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PROTECTION OF CHILD LIFE DURING THE WAR

The General Medical Board of the Advisory Commission of the Council of National Defense early this spring sent out letters to various organizations, requesting the latter to make recommendations indicating in what way they could be of service in the present national crisis. In accordance with this request, representatives of various organizations interested in maternal and child welfare, met in committee at Washington in June, formulated the recommendations given below, and sent them to the General Medical Board.

A glance at the list of societies represented on this committee shows the widespread nature and distribution of the associations interested in infant and child welfare. On the committee are represented not only medical societies and specialists, but also public health and social organizations dealing with these problems.

The chief object of the committee, of course, was to make on a broad, comprehensive scale, recommendations and suggestions looking toward the protection and preservation of the child life of the nation during the war. The recommendations obviously must be of a general nature. The practical application of these recommendations must be left to the individual community, according to the peculiar local conditions of that community.

The report gives evidence of so much thought and expert knowledge, of such care in its preparation, that we believe it will be of universal interest to physicians interested in work among infants and children.—F. S. C.

Washington, D. C., June 15, 1917.

At the request of the General Medical Board of the Advisory Commission of the Council of National Defense the following report of measures recommended for the protection of children in war time is submitted:

1. We urge the Council of National Defense to direct that, so far as practicable, physicians teaching obstetrics and pediatrics and those devoting themselves exclusively to problems of maternity and of infant and child welfare, continue in such service either at home or abroad.

2. Realizing that public health nurses are essential to the carrying on of child welfare work, we recommend that every possible effort be made to prevent these especially trained nurses from being withdrawn from such work, and that public health nursing be officially recognized as war service.

3. Recognizing the increasing need for trained nurses and the inadequate number available for military and home service, we recommend especially

efforts to enlist graduates of colleges and high schools and other suitable candidates for hospital training courses.

4. Organized volunteer aids should be enlisted to assist public health nurses and other social workers through all practicable methods of personal service. We advise appropriate courses of training for such volunteers.

5. We recommend that the Council call on all communities to see to it that there is no abatement, but, on the contrary, a decided increase, in their activities along the lines of maternal, infant, and child welfare—this to apply to all public and private agencies.

6. We deplore the breaking up of the home and recommend that everywhere special provision be made to keep the mother and her young children together in the home; but this does not imply the endorsement of the home work system.

Mothers of nursing infants should be provided for through mothers' pensions or otherwise.

Day nurseries should be especially supervised, and reference should be had to the standards of the National Federation of Day Nurseries. The highest standards should be required of all children's institutions.

7. We urge that the Council of National Defense recommend the prompt enactment of model laws for the registration of births and deaths and the reporting of preventable diseases in the states in which such laws do not exist, and we strongly urge their complete enforcement throughout the country.

8. We urge that every effort be made not only to prevent the repeal or relaxation of any of the existing child labor laws, but we urge on the contrary their more rigid enforcement and the enactment of such further laws as may be needed.

We recommend a plan of supervision similar to that adopted by the National Child Labor Committee in Pamphlets 276 and 277.

9. For the sake of obtaining the highest possible development of child life, and as one of the best means of conserving the character and moral tone as well as physical development of the growing child, we recommend the extension and use of all sound recreational facilities.

10. Appreciating that no plan for real child conservation in war time can be developed without a serious consideration of the mentally defective child and the juvenile delinquent, and especially because of the great increase in juvenile delinquency in Europe since the war, we urge the Council of National Defense to recommend to the various states that greater facilities be created for the recognition and handling of these problems, through the schools, medical teaching, juvenile court work, and children's institutions.

11. We recommend proper medical examination and supervision for boys and girls entering volunteer organizations involving physical exercise.

12. We urge as particularly important the medical examination of boys and girls before they enter industry; also subsequent medical oversight for them.

13. We recommend systematic publicity and free circulation of accredited literature on maternal, infant, and child welfare. Since many organizations are distributing pamphlets and literature broadcast, some good and some poor, we recommend that a committee of obstetricians, pediatricians, sanitarians, and nurses be appointed to review and standardize such literature for wider distribution.

14. We strongly endorse the measures taken by the Army and Navy authorities for the moral protection of the military forces, and endorse also liberal recreational facilities as an indispensable measure to that end.

15. We urge that immediate steps be taken to secure the adoption of a governmental plan to assure adequate support for soldiers and their families. This plan should include financial and medical provision, facilities for the reeducation of the injured soldier, and the reestablishment of the family. Such a plan promptly put into operation would have more effect in promoting child

welfare than any other measure which the government could adopt on behalf of the dependents of men in service.

16. This country should be warned by the mistake of the European countries which have allowed the milk supplies to become impaired. It should therefore take the necessary steps to prevent a milk shortage. We protest against the indiscriminate slaughter of milch cows.

17. We urge the Council of National Defense to ascertain whether there is need among the allied nations for maternity care and infant and child welfare work that can properly be performed by Americans, and if this be the case, that the Council confer with suitable persons or organizations with a view to rendering such service.

18. We recommend that the Council of National Defense organize a national committee representative of maternal, infant, and child welfare associations, to keep in touch during the present emergency with national problems of maternal, infant, and child welfare, and to advise the Council of National Defense from time to time of such features of the then existing situation as may call for remedial action.

We recommend further, that the Council of National Defense, through the several state councils of defense, cooperate with local organizations interested in maternal, infant, and child welfare and establish an agency or appoint an existing agency to secure information as to the specific needs of each community and to show how such needs can be adequately met.

We recommend that so much of this report as may be approved by the Council of National Defense be transmitted to the state councils of defense and to the proposed national and state committees recommended above, if such committees be created, or designated, to guide them in their respective actions looking toward the conservation of maternal, infant, and child welfare during the present emergency.

For the information of the Council of National Defense, a list of those participating in the formulation of this report is appended.

CONFERENCE ON CHILD WELFARE
By (Signed) William C. Woodward,
Chairman.

Memorandum Showing the Official Relations of the Persons Participating in the Formulation of the Attached Report

Dr. F. F. Simpson, Washington, D. C., Chief of Medical Section, Council of National Defense.

Dr. William F. Snow, New York, Assistant Chief of Medical Section, Council of National Defense.

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Dr. Fritz B. Talbot, Boston, American Pediatric Society; Section on Diseases of Children, American Medical Association.

Dr. William Palmer Lucas, San Francisco, American Pediatric Society; Section on Diseases of Children, American Medical Association.

Dr. S. McHamill, Philadelphia, American Association for the Study and Prevention of Infant Mortality; American Pediatric Society.

Dr. Theodore C. Merrill, Sub-Committee on Welfare, Committee on Labor, Advisory Commission of the Council of National Defense.

Dr. J. H. Mason Knox, Jr., Baltimore, American Association for the Study and Prevention of Infant Mortality.

Miss Julia C. Lathrop, Chief, Children's Bureau; Chairman, Child Welfare Committee, Woman's Committee, Advisory Commission of the Council of National Defense.

Dr. Grace L. Meigs, Children's Bureau.

Miss Mary Beard, Chairman, Committee on Nursing, Advisory Commission of the Council of National Defense; Director, Instructive District Nursing Association, Boston.

Mrs. Ellen C. Lombard, United States Bureau of Education.

Dr. William H. Davis, Chief Statistician for Vital Statistics, United States Bureau of the Census.

Miss Mary Dietzler, Washington, D. C.

Miss Gertrude B. Knipp, Executive Secretary, American Association for the Study and Prevention of Infant Mortality, Baltimore.

Mrs. William Putnam, Woman's Municipal League of Boston; Massachusetts Milk Consumers' Association; Vice President, American Association for the Study and Prevention of Infant Mortality.

Mrs. Elmer Blair, Chairman, Public Health Department, General Federation of Women's Clubs.

Dr. Frederick R. Green, Chicago, Council on Health and Public Instruction of the American Medical Association.

Dr. Walter E. Fernald, Superintendent, Massachusetts School for the Feebleminded; Member of National Committee for Mental Hygiene.

Dr. Jessica I. Peixotto, Committee on Children, State Board of Charities and Correction of California; Professor of Social Economics, University of California.

Dr. Frank S. Churchill, Chicago, American Pediatric Society; Section on Diseases of Children of the American Medical Association; Editor, American Journal of Diseases of Children.

FOCAL LESIONS PRODUCED IN THE RABBIT BY COLON BACILLI ISOLATED FROM PYELOCYSTITIS CASES *

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CHICAGO

The mode of infection in pyelocystitis of the infant and child is still far from settled. Much evidence has been brought forward for each of the three routes of infection, the hematogenous, the lymphogenous, and the ascending. In each case the evidence adduced is generalized, and the route of infection made probable by the investigator's observation is claimed as the only possible one. De facto, these observations do not at all preclude the other routes of infection. When we examine the facts as they are at the present time we realize that we do not know what portion of the urinary tract is infected in the condition that is usually termed pyelocystitis. We do know that those cases that come to necropsy usually show some involvement of the kidney pelvis, but that does not prove that a great many of the cases that we see with pus in the catheterized specimen of bladder urine are not merely cases of cystitis. Until these cases are studied more carefully, we must leave this an open question.

Recently the hematogenous mode of infection has been given a great deal of prominence by the work of Cabot and Crabtree,[1] Kowitz[2] and others, who regard the hematogenous route as the only mode of infection. Smith[3] comes to the same conclusion and meets the main argument against the hematogenous mode of infection, the predominance of cases in the female, by assuming that "many cases in the female, accounting for the greater number in this sex as compared with the males, arise from bacteria entering the blood, often via the

* Submitted for publication May 28, 1917.

* From the Otho S. A. Sprague Memorial Institute Laboratory of the Children's Memorial Hospital.

* Read at the meeting of the American Pediatric Society, White Sulphur Springs, W. Va., May 28, 1917.

1. Cabot and Crabtree: Etiology and Pathology of Nontuberculous Renal Infections, Surg., Gyn. and Obst., 1916, p. 495.

2. Kowitz: Ueber bacterielle Erkrankungen der Harnorgane im Säuglingsalter, Jahrb. f. Kinderh., 1915, p. 309.

3. Smith, R. M.: Recent Contributions to the Study of Pyelitis in Infancy, Am. Jour. Dis. Child., 1916, **12,** 273.

lymphatics from the urethra, vulva or vagina." He does not give any evidence, however, in support of this theory, and merely assumes that this may take place.

It seemed to us rather important, therefore, to determine whether or not pyelocystitis could be produced by the hematogenous route. The literature in this connection is very meager. Barlow[4] injected animals intravenously with colon bacilli, without any very definite results. More recently Rosenow's[5] work in the selective localization of bacteria, especially the streptococcus, has called attention to the tendency of bacteria to settle in definite organs. Although his publications do not deal with the colon bacillus alone, he shows that when colon bacilli are injected with streptococci, the tendency is to get lesions in the appendix, gallbladder and intestines. In a series of 31 animals, 26 had lesions in the appendix, 4 of the gallbladder and 13 of the intestine; as compared with only 4 positive findings in a series of 59 animals injected with the streptococci alone. When the colon bacillus alone was injected lesions were very infrequent. This symbiosis is rather interesting when taken in connection with our experiments, in which a mixture of colon bacilli and pneumococci was injected. As in the work of Rosenow, our takes in the kidney were very much more frequent when a mixture of organisms was injected. In order to bring out this difference more strikingly we have kept the two series separate. Series 1 consists of eight different strains of *Bacillus coli* injected intravenously into sixty-six rabbits. Series 2 consists of a mixture of *Bacillus coli* and the pneumococcus injected intravenously into eleven animals.

TECHNIC

The technic employed in the experiments was as follows:

For twenty-four hours before injection the animals were put on a bread and water diet so as to have an acid urine at the time of injection. In every instance the urine was examined before injection for pus cells and albumin. The animals were injected into the ear vein with 0.5 to 1 c.c. of a bacterial suspension, made by centrifuging 15 c.c. of a twenty-four-hour broth culture, and suspending the bacilli in 5 c.c. of salt solution. As indicated in the protocols, the injections were single or repeated.

Series 1: In this series of 66 animals, 26 showed focal lesions of one kind or another. The organs were affected as follows: Kidneys 11 times, cecum 7 times, gallbladder 7 times, appendix 5 times, and stomach 4 times; in addition, there were single instances of hemorrhagic infarction of the descending colon, ulcerative colitis, hemor-

4. Barlow: Cystitis, Arch. f. Dermat. u. Syph., 1893.
5. Rosenow: The Bacteriology of Appendicitis and Its Production by Intravenous Injection of Streptococci and Colon Bacilli, Jour. Infect. Dis., 1915, p. 240.

rhagic enteritis, and duodenal hemorrhage. In Table 2 the positive results have been tabulated.

Taking up the different organs in the order of the table, we find that the appendix was affected in five instances; in two of these there was a typical acute purulent hemorrhagic appendicitis, with gangrene near the base of the appendix in the one. This appendix is shown in Figure 1. In the three other instances the appendix showed considerable subserous edema and numerous small hemorrhages.

The stomach was affected in four instances. In two instances there was an unusual number of small hemorrhages in the mucosa, and in one instance there was a phlegmonous gastritis, most marked at the

TABLE 1.—Characteristics of Organisms Used in Series 1

Organism	Motility	Indol	Gelatin	Litmus Milk	Dextrose	Lactose	Saccharose
B. Coli Communis Injected in:							
B. Series C......	+	+	0	Acid and Coag.	+	+	0
P. Series H......	+	+	0	"	+	+	0
S. Series H......	+	+	0	"	+	+	0
B. Coli Communior Injected in:							
J. P. Series C, D and E	+	+	0	"	+	+	+
C. Series L......	+	+	0	"	+	+	+
L. Series C......	+	+	0	"	+	+	+
B. Series F and G	+	+	0	"	+	+	+
B. Paracolon Injected in:							
E. Series C......	+	+	0	Acid; alk. after 48 hours	+	0	0
L. Series H......	+	+	0	"	+	+	0
Organisms used in Series 2							
B. Coli Communior and Pneumococcus	+	+	0	Acid and Coag.	+	+	+

pyloric end and involving almost one-half of the stomach. The stomach wall was immensely thickened and edematous, especially the muscular coats, and microscopic sections showed diffuse leukocytic infiltration and edema. The fourth instance was a typical gastric ulcer, with a markedly edematous margin, and numerous small hemorrhages in the base. Cultures from the surface of the ulcer and deep down in the tissues yielded only a colon bacillus. This organism was reinjected into a series of animals without producing an ulcer in any one of them.

The gallbladder was affected seven times. The lesions varied from a slight thickening, with minute hemorrhages, to a purulent cholecystitis with fibropurulent gluing together of the stomach, colon and liver. The relatively large number of rabbits that showed coccidiosis

of the gallbladder may account for the number of gallbladder infections that were produced.

The cecum was involved in seven instances. The lesion was a peculiar edematous induration that involved only a few centimeters of the cecum or extended over from 12 to 15 cm. of the entire wall. Figure 2 shows very well the peculiar edematous swelling of the entire wall and also the peculiar hemorrhagic necroses at the tops of the folds

Fig. 1.—Hemorrhagic appendicitis.

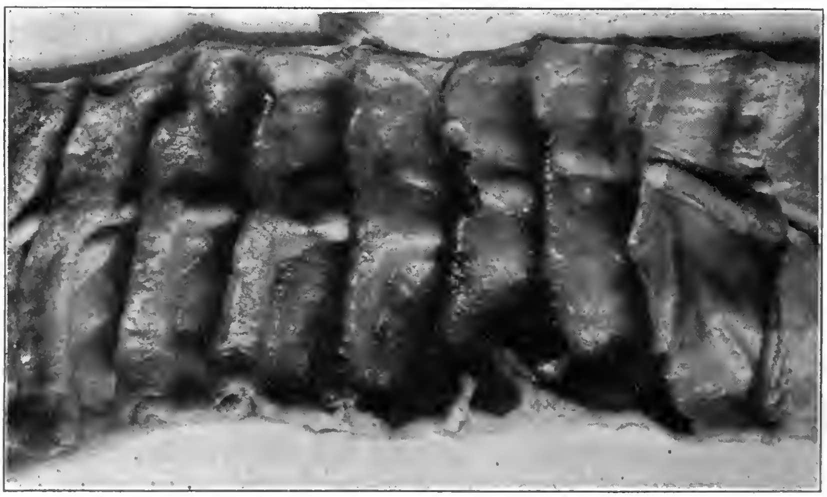

Fig. 2.—Edematous induration of the cecum.

of the mucous membrane. In several instances a diphtheritic exudate could be seen on the tips of the folds. In some the edema was the most marked condition; in others the hemorrhagic condition of the mucous membrane. On section, the lesions proved to be a tremendous inflammatory edema with necrosis of a large portion of the mucous membrane at the tips of the folds. There was also to be seen an inflammatory exudate on the peritoneal surface.

No.	Animal	Date	Source and Amount Injected, C.c.	Days Until Death	Appendix	Stomach	Gall-bladder	Cecum	Kidney: Hemorrhage	Kidney: Cortical Abs.	Kidney: Medullary Abs.	Kidney: Pyelitis	Urine: Albumin	Urine: Pus	Culture Colon	Remarks
1	R 1X....	5/23 5/24	½ R1V.. ½........	D 4	+	+	0	0	0	0	+	0	+	0	+	Phlegmonous gastritis; pel. culture, gram negative bacillus
2	R X.....	5/23 5/24	½ R1V.. ½........	D 3	0	0	0	+	0	0	+	0	+	..	+	Pelvis culture, gram negative bacillus
3	R X111..	5/27	1 RX....	D 1	0	0	0	+	0	+	+	0	+	..	..	Necropsy 24 hours after death
4	R 2D....	5/30 5/31	⅕........ 1 R1X...	D 3	0	0	0	+	0	+	0	0	..	0	+	
5	R 3D....	5/30 5/31	⅕ R1X.. 1........	S 3	0	+	0	0	0	0	0	0	..	..	0	Stomach ulcer; pure culture, gram negative bacillus from base of ulcer
6	R 4D	5/30 5/31	½ R1X.. 1........	S 3	0	0	+	0	0	0	0	0	..	..	..	Culture of gallbladder, pure gram negative bacillus
7	R 5D....	5/30 5/31	1/10 R1V ½ app...	S 4	0	0	+	0	0	0	0	0	..	0	+	Culture of gallbladder, pure gram negative bacillus
8	R 6D....	5/30 5/31	⅕ app... ½........	D 2	0	0	0	0	0	0	0	0	+	0	..	Hemorrhagic infarct. of desc. colon; kidney culture, pure gram negative bacillus
9	R 10D...	5/30 5/31	⅕ app... ½........	D 2	0	0	0	+	0	0	0	0	..	..	..	Peritonitis; hemorrhage in bladder
10	R 11D...	5/30 5/31	⅕ app... 1........	S 4	0	0	0	0	0	0	0	0	+	+	+	Hemorrhage in bladder
11	R 1E....	6/ 3	½ R4D..	S 3	0	0	+	0	0	0	0	0	..	..	..	
12	R 2E....	6/ 3	1 R4D...	D 3	0	0	+	0	+	0	0	0	..	..	..	
13	R 4E....	6/ 3	½ R3D..	D 2	0	0	0	+	0	0	0	0	..	..	..	
14	R 1H....	6/21	1 N. L...	D 2	+	0	0	0	+	0	0	0	..	..	0	
15	R 2H....	6/21	1 N. L...	D 2	+	0	0	0	0	0	0	0	..	..	..	Peritonitis
16	R 5H....	6/22	1........ Perin....	Dying D 1	+	0	0	0	0	0	0	0	0	0	+	Marked hemorrhage into duodenum
17	R 9H....	6/23	1........ Sullivan	D 1	+	0	0	+	0	0	0	0	0	0	..	Hemorrhagic enteritis
18	R 11H...	6/26	Bl. of... R8H.....	Dying 1 S	0	+	0	0	0	0	0	0	0	0	0	Enteritis; hemorrhage in duodenum
19	R 2K....	6/28	Bl. R7G. 1........	S 5	0	0	0	0	0	0	0	+	+	R O L +	+ ..	Pus from left, clear urine from right ureter
20	R 6K....	6/28	Bl. R7G. 1........	S 5	0	0	+	0	0	0	0	+	+	R + L O	+ ..	Pus from right ureter; clear urine from left
21	R 7K....	6/28	Bl. R7G. ½........	D 2	0	0	0	+	0	+	+	0	0	0	+	Peritonitis
22	R 15K...	7/ 4	Bl. R2K. 1........	D 3	0	0	0	0	0	0	0	0	+	+	..	Ulcerative vaginitis
23	R 17K...	7/ 4	Bl. R2K. 1........	D 4	0	0	+	0	0	0	0	0	..	..	..	
24	R 1L....	7/12	3........	S 4	0	0	+	0	0	0	0	0	0	0	..	
25	R 3L....	7/13	½ cult...	D 2	0	+	0	0	0	0	+	0	+	+	..	
26	R 4L....	7/13	¼ cult...	D 1	0 *5	0 *4	0 *7	0 *7	+ *3	0 *3	0 *5	0 *2	+ *10	0 *5	0 ..	Infection of colon

The kidney showed focal lesions eleven times; inasmuch as three of these were only hemorrhages of very slight extent, in two of the instances only seen microscopically, it must be considered doubtful whether they have any definite relationship to the colon bacillus injections. The remaining eight animals showed kidney lesions as follows: three had cortical abscesses, three had medullary abscesses, and two had a unilateral pyelitis.

Cortical Abscesses. — In one rabbit the cortical abscesses were apparently of very recent origin and had not spread along the tubules, down into the medulla. In the other two, the abscesses had involved the medulla also. In one of these animals the abscesses were visible

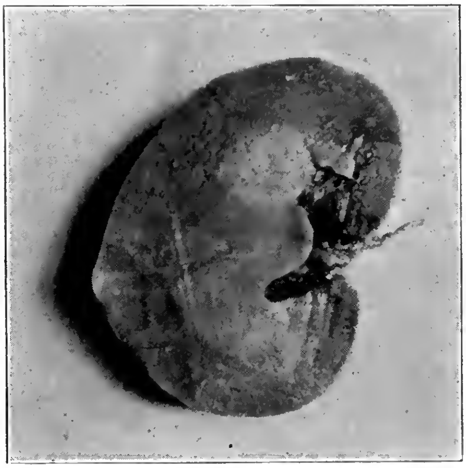

Fig. 3.—Cortical abscesses.

to the naked eye as small, opaque, yellowish nodules in the surface of the kidney, which on section could be seen extending down into the medulla, as seen in Figure 3. In the other of these two animals, the lesions were only discovered in the microscopic examination of the kidney section. The abscesses in the cortex were very minute, involving one or two glomeruli, and those in the medulla showed a tubule or two filled with pus, about which there was some infiltration. The pelves in both of these cases were normal in the sections examined.

Medullary Abscesses.—Two of the three cases showed practically the same condition, a practically normal, reddish-brown kidney externally, and on section, small, yellowish, opaque nodules in the medullary portion of the kidney. These proved to be minute abscesses in which numerous bacilli could be demonstrated. The third rabbit showed a very different picture; the kidney was very much swollen and slightly discolored by postmortem changes, but showed in spite of that, very

extensive abscesses in the medulla; the cortex as far as abscess foundation went was practically intact. The medulla was fairly studded with abscesses extending down along the tubules as seen in Figure 4.

Pyelitis.—Of the sixty-six animals injected, only two showed a typical pyelitis, and in both instances the pyelitis was unilateral. In both instances pus could be expressed from one ureter and clear urine from the other; and on section of the kidney pus welled out of the pelvis in one and a small amount of clear urine out of the other. Histologically, the kidneys of the unaffected and affected side were practically identical, except that in the one the pelvis was filled with pus; in the other not. Changes in the wall of the pelvis were manifest only in an excessive number of polymorphonuclear cells in certain areas.

Fig. 4.—Medullary abscesses.

The question naturally arises at this point as to what the primary lesion is in pyelitis, and why should one get a unilateral pyelitis in these two cases? It emphasizes the fact that unilateral pyelitis does not necessarily point toward the lymphatic mode of infection, but that bacteria may lodge in one kidney and grow, and not in the other even when larger doses are given intravenously than could ever be conceived of in human pathology.

SERIES 2: Over against Series 1 we wish briefly to summarize experiments of Series 2 (Table 3), consisting of eleven animals which were injected with a mixed culture of pneumococci and colon bacilli isolated from a severe case of bronchitis and pyelitis, in which on catheterization only a glass catheter full of practically pure pus could be obtained just before death. Of the eleven animals injected, six showed focal lesions of the kidney; three had a pyelitis; one had cortical abscesses, and two had diffuse hemorrhages in the cortex.

TABLE 3.—Data of Experiments in Series 2

No.	Animal	Date	Source and Amount Injected, C.c.	Days Until Death	Appendix	Stomach	Gallbladder	Cecum	Kidney: Hemorrhage	Kidney: Cortical Abs.	Kidney: Medullary Abs.	Kidney: Pyelitis	Urine: Albumin	Urine: Pus	Urine: Culture Colon	Remarks
1	R 2F...	6/ 9	S & C... 1.........	S 8	0	0	0	..	..	..	..	+	+	+	C + P +	
2	R 3F....	6/ 9	S & C... ½........	S 6	..	..	+	..	..	+	..	..	+	+	C + P +	Pericarditis; culture, pure pneumococcus; pneum. and colon from pelvis of both kidneys
3	R 4F....	6/ 9	S & C... 1 B......	S 8	0	0	0	0	0	0	0	+	+	+	C + P +	
4	R 39G...	6/17	S & C... 1 Kid. of R3F	D 2	+	0	0	+	+	0	0	0	..	0	C +	Pure culture B. coli from appendix; culture from kidney cortex negative
5	R 49G...	6/19	S & C... 1 Kid. of R3F	S 2	0	+	0	0	+	0	0	0	+	0	0	
7	R 79G...	6/20	S & C... 1 Kid. of R3F	Dying 7 S	0	0	0	0	0	0	0	+	+	+	C +	
					*1	*1	*1	*1	*2	*1	*0	*3	*5	*4	..	

* Totals.

The hemorrhages in the one were very severe, as over two-thirds of the kidney surface was hemorrhagic; in the other the hemorrhages, though less severe, were more marked than in any of the rabbits injected with colon bacilli alone.

Cortical Abscesses.—In the one case with cortical abscesses the lesion was very widespread. There were large, yellow, raised areas on the surface of the kidney that extended down in wedge-shaped areas to the tips of the papilla.

Pyelitis.—Of the three cases of pyelitis, one must be put in the doubtful column, because the diagnosis of pyelitis rested on the finding of masses of pus cells in the pelvis of the kidney as well as in the cross-section of the ureter histologically, without having found any in the specimens of urine examined, and without any findings macroscopically at necropsy. In the second there were pus cells in the urine, but a practically empty pelvis at necropsy. Histologically, however, there were seen in section definite areas of leukocytic infiltration in the pelvis wall.

In the third case the kidney substance was normal in both, except that the medulla looked somewhat edematous; the pelvis in both kidneys exuded thick creamy pus when opened up. The pelvic mucous membrane was practically intact in the sections studied, but the lumen of the pelvis was filled with a solid mass of polymorphonuclear leukocytes, red blood cells and mononuclear cells.

These three cases emphasize again the difficulty of a study of pyelitis. The first two would have been simply overlooked if sections had not been studied, and it is readily conceivable that a section taken in another portion of the kidney would not have showed these changes.

As controls for these experiments, we injected four different strains of colon bacilli isolated from the intestinal canal of infants suffering from slight intestinal disturbances. Three animals were injected with each strain. Of the twelve injected, in only one animal were there any local findings. This was a purulent appendicitis. The urinary examinations in all the animals were entirely negative; not a single animal showed pus or albumin in any of the examinations made.

The results of the experiments were a considerable surprise. We had anticipated a much larger series of takes in the kidney than were obtained. In Series 1, of the sixty-six animals injected, only eight, about 12 per cent., showed lesions that could be attributed to the *Bacillus coli.* In the same series the appendix was involved 5 times, the stomach 4 times, the gallbladder and the cecum each 7 times. It is thus evident that of the eight organisms used, none showed a special tendency to localize in the kidney, and when it did localize the focal lesions were just as likely to be in other organs, especially the gastro-

intestinal tract. The most characteristic lesion of the colon bacillus appeared to be the edematous infiltration of the cecum. It would seem that the rabbit in almost 90 per cent. of instances can excrete colon bacilli through the kidney without any harm to the kidney. If we compare this with the results obtained by injecting a mixture of pneumococci and colon bacilli, we find that the kidney is more frequently affected. In six out of eleven rabbits, or in 60 per cent., the mixture caused definite lesions in the kidney. This increase of focal lesions corresponds closely to the difference in appendiceal localization described by Rosenow, when a mixture of colon bacilli and streptococci was injected. The question naturally arises whether in human pyelocystitis there is frequently a double infection. The second organism may be easily overlooked, because cultures are usually not made early when both organisms would most likely be present, and if present the colon bacillus tends to overgrow the other. In two cases of hematogenous streptococcus pyelitis in the rabbit we could observe that the colon bacillus made its appearance later, and still later completely displaced the streptococcus.

CONCLUSIONS

1. It is possible to produce typical pyelocystitis in the rabbit by the intravenous injection of colon bacilli isolated from human cases.

2. If a mixture of organisms is injected, the relative number of kidney infections can be greatly increased.

PROTOCOLS

Rabbit 1X.—Weight, 1 pound 3¼ ounces.

May 23, 1916. Urine dark yellow; amorphous precipitate; alkaline. Microscopic: amorphous precipitate; 0.5 c.c. bladder culture of Rabbit 1V injected intravenously; bread diet.

May 24. Urine acid; negative; 0.25 c.c. bladder culture Rabbit 1V reinjected intravenously.

May 25. Urine dark yellow, thick, slightly cloudy, strongly acid, slight trace of albumin. Microscopic: few cells; no precipitate; no bacteria. Stained urine, no bacteria.

May 26. Urine yellow, cloudy, thick, acid; albumin +.

May 27. Rabbit died.

Necropsy.—On opening the peritoneum there is a fibrinous exudate over the upper portion of the abdominal cavity. The stomach is deeply injected and also the ascending portion of the duodenum. The appendix is about the size of a little finger, firm, of yellowish opaque color, deeply injected, in one area greenish black and necrotic looking. On opening the appendix the wall is thickened and hemorrhagic. The lumen is filled with hemorrhagic, yellowish-brown detritus. The duodenum on opening shows areas in which there have been numerous hemorrhages. The stomach wall is intensely thickened and edematous in the pyloric region, less markedly so in the cardiac end. The kidneys are of a brownish-red color, the capsule strips readily. There is nothing unusual externally. On section midway between cortex and papilla there are numerous fine yellowish streaks and spots about 1 mm. across.

May 29. All cultures were of an atypical colon bacillus. Bladder urine acid; no excess of cells; albumin + +.

Histology.—Section 5: The stomach shows an enormous edematous swelling of the submucosa. Most of the cells in the edematous area are lymphocytes. There are numerous hemorrhages into the muscularis.

Section 3: The pancreas and duodenum show marked hemorrhages into the submucosa; also in the muscle and parenchyma. The tissues are well preserved.

Section 4: The liver is negative except for cloudy swelling.

Section 5: Appendix. There is no mucosa left. There is massive infiltration of the lymphatic tissue, with a large area of necrosis and hemorrhages. The muscle layer is densely infiltrated.

Section 6: Kidney. There are miliary abscesses in the central portion of the medullary portion. The medulla in large area is densely infiltrated with lymphocytes, separating the collecting tubules. The cortex shows only slight swelling. There are no hemorrhages.

Rabbit X.—Weight, 1 pound 3 ounces.

May 23. Urine clear; slight amount of phosphate precipitate. Microscopic: no cells; no albumin; alkaline; 0.5 c.c. bladder culture Rabbit 1V injected intravenously; bread diet.

May 24. Urine acid, negative. Reinjected with 0.5 c.c. bladder culture from Rabbit 1V.

May 25. Urine bright yellow, clear, acid; albumin, a trace. Microscopic: no cells; slight precipitate; no bacteria; stained urine, no bacteria.

May 26. Died.

Necropsy.—No distention of bladder. Bladder and pelvis of right kidney were cultured. The kidneys are of reddish-brown color, with no external changes. The capsule strips readily. On section the cortex is slightly more opaque than usual. There is no mottling. The pyramids, beginning about the middle, are studded with small yellowish opaque dots and streaks extending down toward the papilla; the pelvis is everywhere smooth. No injection or hemorrhage is to be made out in either kidney. The lungs and heart were negative. The other organs were negative.

May 29. Pelvis of kidney and bladder yielded a pure culture of colon bacillus. (J. P.)

Rabbit X111.— May 27. Bladder culture from Rabbit X injected intravenously. Urine acid, clear, pale, straw color; albumin, 0.

May 28. Died.

Necropsy.—A loop of colon is covered with tags of purulent exudate, markedly injected, and a hemorrhage on the surface covers an area 2 cm. in diameter. Appendix normal; heart and lungs, and kidneys negative on macroscopic examination.

Histology.—Kidney: There are miliary abscesses in the cortex involving several glomeruli; glomeruli filled with pus cells. In the tubules of the medulla near the tip of the pyramid are several tubules distended with a purulent exudate. One has extended to the tissue between the tubules. In the same portions of the kidney there are tubules filled with masses of bacilli. The pelvis of the kidney shows no change. Colon: The tissue is infiltrated with red blood corpuscles and almost entirely necrotic; only the muscular layer still shows nuclear stain.

Rabbit 2D.—Weight, 15 ounces.

May 30. Cultures of kidney of Rabbit 1X, 0.2 c.c. injected intravenously. Urine entirely negative on examination.

May 31. Reinjected, 1 c.c.

June 2. Died.

Necropsy.—On opening the peritoneal cavity the cecum just at the ileocecal

valve is thickened and hemorrhagic; on opening up this portion of the cecum it is seen to be edematous. The wall is considerably infiltrated, the rugae thickened and numerous hemorrhages on the mucous surface. The kidneys are smooth, of a brownish-red color, and show just under the capsule numerous yellow, opaque nodules about 5 mm. in diameter. The bladder shows some hyperemia of the walls. The gallbladder lies free, studded with white areas similar to Rabbit 4D but not so marked. The other organs are normal.

The urine shows casts and a large number of epithelial cells. Cultures from bladder and cortex of kidney give a colon bacillus.

Histology.—Cecum: There is practically a phlegmon of the entire wall. The submucosa is rich with purulent exudate; mucosa hemorrhagic; only few acini of epithelium remain; muscularis infiltrated with pus cells.

Rabbit 3D.—Weight, 15½ ounces.

May 30. One c.c. culture from kidney of Rabbit 1X injected.

May 31. One c.c. reinjected.

June 2. Sacrificed.

Necropsy.—The abdominal cavity is entirely negative, the cecum and appendix are normal. The bladder is distended. The stomach and duodenum are normal externally. On opening the stomach the cut passes through an ulcer, measuring about 4 mm. across. The ulcer is sharply defined, with a yellowish base, in which are numerous hemorrhages; the edges are thickened, markedly edematous and somewhat wavy. The base is on the muscular layer. Cultures from base and edematous area around the ulcer gave a gram-negative bacillus, an atypical colon bacillus, as was the original J. P. organism. The bladder culture was negative.

Histology.—Section of Kidney: Marked cloudy swelling and vacuolar degeneration of parenchyma. Medulla and pelvis normal. In some areas, apparent necrosis of epithelium.

Stomach: The ulcer shows very intense reaction about it; very marked edema and polymorphonuclear infiltration. In the ulcer base there are a considerable number of red blood corpuscles. The serosa is intact, although there is considerable infiltration just below it.

Rabbit 4D.—Weight, 15½ ounces.

May 30. One-half c.c. of culture from kidney of Rabbit 1X injected.

May 31. One c.c. injected.

June 2. Sacrificed.

Necropsy.—Findings normal in urinary and gastro-intestinal canal. Gallbladder on external surface hemorrhagic and of an opaque yellowish color. Material removed from it contains large numbers of leukocytes and many gram-negative bacilli. Pus from gallbladder when cultured gave pure culture of gram-negative bacilli—an atypical colon organism similar to the organism originally cultivated from J. P.

Histology.—Section of Kidney: Marked cloudy swelling and vacuolar degeneration. In medulla two-thirds of way to top of pyramid is a small hemorrhage.

Rabbit 5D.—Weight, 12¼ ounces.

May 30. One-tenth c.c. of culture from appendix of Rabbit 1X injected.

May 31. One-half c.c. reinjected.

June 3. Sacrificed.

Necropsy.—On opening the peritoneal cavity the bladder is markedly distended with reddish yellow urine. On folding back, the cecum is adherent to the lower surface of the liver. On peeling back, the stomach, too, is seen to adhere to the lower surface of the liver. These adhesions all seem to be around the gallbladder, extending for some distance along the cecum. The adhesions are of darkish, brownish yellow color, and completely encapsulate the gallbladder, which is covered by the same sort of a fibrinous exudate in its sulcus in the liver. The gallbladder is tense and red where the exudate

has been stripped off. Puncture of the gallbladder shows it to contain a yellowish, thinly purulent material. The smear of contents shows gram-negative bacilli. Kidneys: Slightly enlarged, yellowish-brown, slightly mottled, and on section show a thickening of the cortex. The pyramids and pelves are normal. Cultures from gallbladder and bladder show gram-negative bacilli.

Histology.—Kidney: Intense degeneration of cortex; in some areas, complete necrosis of parenchyma; pelvis and medulla negative.

Rabbit 6D.—Weight, 8½ ounces.

May 30. One-fifth c.c. of appendix of Rabbit 1X injected.

May 31. One-half c.c. reinjected.

June 1. Died.

Necropsy.—Hemorrhagic infarction of descending colon; otherwise negative; culture of kidney shows a gram-negative bacillus. Urine: A few cells; much debris; faintly acid; albumin + +.

Histology.—Descending colon: The entire section is completely infiltrated with red blood corpuscles. The nuclei of the muscles and epithelium are still to be made out. The kidney shows cloudy swelling; otherwise negative.

Rabbit 10D.—Weight, 17½ ounces.

May 30. One-fifth c.c. of culture from appendix of Rabbit 1X injected.

May 31. One c.c. reinjected.

June 1. Died.

Necropsy.—The abdomen is distended. On opening there is an excess of fluid in the peritoneum. The cecum is hemorrhagic and for about 5 inches is covered with fibrinous shreds. The wall is markedly thickened. On opening, the wall is seen to be edematous, the folds hemorrhagic. The remainder of the bowel is injected only where in contact with the cecum. The stomach and duodenum are normal. The kidneys are negative. Cultures from kidney and cecum give gram-negative bacilli. Section 1: Cecum. The mucosa is infiltrated with pus cells and serum. The submucosa is thickened and infiltrated with masses of pus cells.

Rabbit 11D.—Weight, 18 ounces.

May 30. One c.c. of culture of appendix of Rabbit 1X injected.

May 31. One c.c. reinjected.

June 3. Sacrificed.

Necropsy.—The appendix and cecum are normal. The bladder is distended with cloudy urine. The urine contains large numbers of individual cells and masses of cells. On opening the bladder it is seen to be somewhat thickened, hyperemic and has a few hemorrhages. The kidneys are negative externally and on section; the pelvis is normal. Other organs are negative. Culture from bladder, gram-negative bacilli.

Histology.—The kidney shows cloudy swelling. One area has blood on surface of pelvis and no epithelium, probably a postmortem change. The bladder shows marked infiltration with polymorphonuclear leukocytes; hemorrhages and edema.

Rabbit 1E.—Weight, 1 pound 10½ ounces.

June 3. One-half c.c. of gallbladder culture of Rabbit 4D injected.

June 6. Sacrificed.

Necropsy.—Appendix normal; all organs normal. The gallbladder is somewhat thickened and contains thin fluid of a light yellowish color, with numerous white opaque follicles. It is slightly reddened in areas. A smear of the contents shows gram-negative bacilli. Culture shows pure gram-negative bacilli.

Histology.—Kidneys negative, except for marked cloudy swelling. The gallbladder shows areas of necrosis in the wall, with leukocytic infiltration, edema and hemorrhages.

Rabbit 2E.—Weight, 1 pound 12 ounces.

June 3. One c.c. of culture from gallbladder of Rabbit 4D injected.
June 6. Died.

Necropsy.—On opening the peritoneal cavity the upper third of the abdominal organs are seen to be adherent to the parietal peritoneum. The loops of the bowel are injected and glued together and to the liver and stomach. The upper portion of the cecum, in like manner, is glued to the stomach. The liver on its under surface over the region of the bile duct adheres to the stomach and is covered with a brownish-yellow, thick exudate. The omentum is hemorrhagic covering over the stomach. The gallbladder is encased in a sheath of fibrinous exudate which can be peeled back and shows a somewhat distended gallbladder. The adjacent surfaces of the liver also are covered with the exudate. The portion of the stomach adjacent to the liver is injected, and about the pyloris it is considerably thickened and indurated. The inner surface of the stomach shows nothing abnormal. The portion of the bowel which is externally inflamed shows nothing on its internal surface. The cecum and appendix are normal; kidneys normal; heart and lungs normal. There is some stippling of the gallbladder as though of coccidial origin. Cultures made of the gallbladder and intestinal wall show gram-negative bacilli.

Histology.—The heart muscle is negative. There is a large hemorrhage in the kidney at the junction of the cortex and medulla.

Rabbit 4E.—Weight, 1 pound 1¾ ounces.
June 3. One-half c.c. of culture from ulcer of Rabbit 3D injected.
June 5. Died.

Necropsy.—On opening the peritoneal cavity the descending colon and rectum are found thickened, much injected and covered with fibrinous exudate. The cecum at the ileocecal valve shows several areas of minute hemorrhages. Under these areas are seen hemorrhages into one of the folds of the mucous membrane. The stomach and gallbladder are normal; also the kidneys.

Histology.—Cecum: The mucosa is intact. There are marked diffuse and focal hemorrhages into the submucosa and muscularis, but no excess of leukocytes. The edema is marked. Kidney: There is marked cloudy swelling and congestion of the medulla, especially of the pyramidal tips. The pelvis is absolutely negative.

H Series: Rabbit H1.—Weight, 1 pound 15½ ounces.
June 21. One c.c. of culture from urine of N. L. injected.
June 21. Urine alkaline; no cells; albumin, 0.
June 22. Rabbit very ill; diarrhea.
June 23. Died.

Necropsy.—Acute hemorrhagic appendicitis. The appendix shows a few peculiar opaque areas near the top. There are minute hemorrhages in both kidneys and a few depressions on the kidney surface. Bladder culture is negative.

Histology.—Numerous hemorrhages in cortex of the kidney, and blood corpuscles in a few of the collecting tubules. The pelvis is negative.

Rabbit 2H.—Weight, 2 pounds ¼ ounce.
June 21. One c.c. of culture from urine of N. L. injected. Urine acid; crystalline precipitate; no cells; albumin ±.
June 22. Abdomen hard; pain when effort was made to express urine.
June 23. Dead.

Necropsy.—A purulent peritonitis was found. The culture of peritoneum shows a pure gram-negative bacillus. The appendix shows marked proliferation of the epithelial cells and phagocytosis of lymphatic cells; no hemorrhages.

Rabbit H5.—Weight, 1 pound 5½ ounces.
June 22. One c.c. of culture from urine of P. injected. Urinary examination entirely negative.
June 23. Dying. Diarrhea.

Necropsy.—Marked distention with fluid of the intestines, and all along the intestinal canal are hemorrhages. The appendix shows numerous hemorrhages along the course but most marked at its attachment to the cecum. The appendix is filled with fecal material, moist at proximal end, dry at the tip. The mucous membrane is intact. The stomach is normal but there are marked hemorrhages into the duodenum. Culture of bladder gives gram-negative bacilli. Examination of urine negative; no albumin.

Histology.—Duodenum: Hemorrhages into mucosa and submucosa. No inflammatory reaction of leukocytes. The mucous membrane is gone in the hemorrhagic areas, although glands deep down remain. The kidney has cloudy swelling. The pelvis of the kidney is intact, showing no excess of cells.

Rabbit H9.—Weight, 1 pound 1¼ ounces.

June 23. One c.c. of culture from urine of S. injected. Urine alkaline; microscopically negative; no albumin.

June 24. Died. Marked diarrhea.

Necropsy.—The bowel is filled with liquid contents. There are numerous hemorrhages on the appendix, especially toward its base. There are a few hemorrhages into the cecum and numerous hemorrhages into the upper portion of the intestine. There was a hemorrhagic enteritis of the upper portion of the ileum. In this area the ileum is filled with hemorrhagic mucopurulent material. The kidneys and gallbladder are negative. Stomach, duodenum and heart are negative.

Histology.—The ileum shows hemorrhages into the mucosa and inflammatory exudate in the submucosa.

Rabbit H11.—Weight, 1 pound 2½ ounces.

June 24. Injected with bladder culture from Rabbit H8; 1 c.c. given.

June 26. Urine examined; cloudy, acid, microscopically negative; albumin negative.

June 27. Animal almost dead; sacrificed. There is no excess of fluid. In peritoneal cavity the organs are normal. The exterior of the duodenum shows a few hemorrhages. The ileum is distended with fluid and shows injection and scattered small hemorrhages. On opening there are hemorrhages (minute in stomach, larger in duodenum) and throughout a large portion of the ileum. The kidneys are yellowish brown and somewhat fatty. The pelvis is negative. The bladder is negative.

Histology.—The kidney shows cloudy swelling. The appendix and stomach show nothing of note.

K. Series: Rabbit 2K.—Weight, 12½ ounces.

June 28. One c.c. of bladder culture of Rabbit 7G injected. Urine examined before injecting. Microscopically negative; acid; albumin 0.

June 30. Urine acid; single cells and numerous clumps; a few casts; albumin +.

July 3. Urine acid; many cells and groups of cells; sacrificed. Bladder apparently normal; ureters small, apparently normal. The urine expressed from the right ureter negative; from left, yields pus. The kidneys externally are smooth and of a brownish-red color. On section the right kidney is normal. Cortex and medulla are normal and there is no pus in the pelvis, which appears normal. The left kidney is the same as the right, except that there is pus in the pelvis. Bladder cultured; pure gram-negative bacillus found. Smear of pus from left ureter contains pus cells and gram-negative bacilli.

Histology.—Left Kidney: The cortex, except for cloudy swelling, is normal. The medulla shows nothing unusual. The pelvis is filled with masses of pus cells. In parts, especially on the papilla, the mucous membrane is intact. On the surface of pelvis there is a loss of mucosa for a considerable area; in parts small islands of squamous epithelium remain. On one side is seen a large vessel with a thrombus in it. There is a marked infiltration of the mucous membrane with eosinophils. The right kidney is negative; bladder negative.

Rabbit 6K.—Weight, 1 pound 2¼ ounces.

June 28. One and one-half c.c. of culture from bladder of Rabbit 7G injected. Urine examined; microscopically negative; acid; albumin 0.

June 30. Large amount of dark urine; many hyaline and granular casts; precipitate contains no excess of cells; albumin present.

July 3. Sacrificed. Bladder urine contained pus cells. The rabbit seems in excellent condition. On opening the peritoneum, the bladder is practically empty, the stomach and intestines normal. The gallbladder is covered in the lower half with a fibrinous purulent membrane adherent to the liver. The appendix, stomach and duodenum are normal. The bladder contains a small amount of urine, with excess of pus cells, single and in clusters. The urine expressed from the cut ureter on the right side yields pure pus; on the left side very few epithelial cells. A smear of the pus from right ureter contains gram-negative bacilli. A smear of urine from bladder shows a gram-negative bacillus in pure culture. The right kidney is of a brownish yellow color and smooth on section. The pelvis of the kidney exudes thick yellow pus. The cortex is opaque and yellow; the medulla shows nothing unusual. The left kidney on section shows no pus in the medulla, but in every other way resembles the right. The ureter of the right kidney is considerably smaller. Cultures of gallbladder contents shows a gram-negative bacillus.

Histology.—The epithelium on the pyramid is intact; over the opposite side of the pelvis the epithelium is lost and the surface is made up of a mass of pus cells. There is considerable infiltration of the lining of the pelvis. In the left kidney there is no pus in the pelvis, but a slight increase in connective tissue in the cortex. The bladder is negative.

Rabbit 7K.—Weight, 1 pound 11¾ ounces.

June 28. One and one-half c.c. of bladder culture of Rabbit 7G injected; Urine examined; a few cells and no albumin were found.

June 30. Died.

Necropsy made immediately after death. Peritonitis present; excess fluid; coccidiosis, especially about stomach and duodenum. Bladder contains a small amount of normal urine. Left kidney shows two small yellow opaque areas in cortex. Otherwise negative except for the injection of a portion of cecum near valve. Culture of bladder heavy growth in broth of gram-negative bacillus.

Histology.—There are minute abscesses in kidney, both in the cortex and the medulla.

Rabbit 15K.—Weight, 1 pound 4½ ounces.

July 4. One c.c. of bladder culture from Rabbit 2K injected. Urine examined; microscopically negative, acid; albumin 0.

July 5. Diarrhea; many pus cells and epithelial cells; acid, albumin ++.

July 6. Diarrhea; many pus cells and groups of cells; acid; albumin ++.

July 7. (Weight 15½ ounces; ill); urine loaded with pus cells and groups of cells; acid; albumin ++.

Died between July 7 and 8.

Necropsy.—On opening the peritoneum, hemorrhages are found in the lower portion of the retrovesical tissue; bladder distended with large amount of urine, which does not contain excess of pus cells. Bladder wall on top shows slight thickening; kidneys normal. Stomach and duodenum normal. Gallbladder adhered to the liver and covered with omentum, which is matted together and can be separated from the gallbladder in a thickly purulent area. Along the line of cleavage there is a purulent membrane; appendix, stomach and duodenum normal. Heart negative. Kidneys smooth, uniform in color, on section show nothing unusual. Coccidiosis of liver and gallbladder. Vagina much reddened, and in an area about 3 mm. across there is an opaque, yellowish membrane.

Histology.—The kidneys show nothing abnormal. The vagina shows a pseudomembranous inflammation of the wall, with considerable necrosis.

Rabbit 17K.—Weight 1 pound 8¼ ounces.

July 4. One c.c. of bladder culture of Rabbit 2K injected. Urine examined; microscopically negative; acid; albumin 0.

July 5. Diarrhea. About 20 c.c. of urine expressed; contains a few cells and groups of cells, probably no excess; acid; albumin +.

July 6. Diarrhea; no excess of cells; acid; albumin 0.

July 7. Weight, 1 pound 3½ ounces. Urine examined, negative; cloudy with amorphous precipitate; acid; no albumin.

July 8. Died.

Necropsy.—On opening there is an excess of fluid in the peritoneum. The bladder is markedly distended; the intestinal canal is apparently normal; kidneys are smooth, of a uniform color on the surface. The gallbladder is studded with white opaque areas, and in addition numerous small hemorrhagic areas. The gallbladder is smooth on the external surface. The kidney on section shows nothing unusual. The pelvis is smooth and contains no pus. Nothing is obtained from the ureters.

Histology.—The kidneys show nothing of note.

Series L: Rabbit L1.—Weight, 2 pounds.

July 12. Three c.c. of a sodium chlorid suspension of bacilli from the urine of C. injected. Suspension approximately the same as in the urine. Urine examined; a few cells; urine clear, alkaline; acid to phenolphthalein; no albumin.

July 13. No excess of cells; acid; albumin 0.

July 14. A few cells; acid; albumin +.

July 15. Large number of pus cells; acid; slight amount of albumin. Sacrificed.

Necropsy.—Bladder urine negative; no pus obtained from either ureter; kidneys are negative; no vaginitis. The gallbladder is hemorrhagic, infected and full of pus. The findings otherwise are entirely negative.

Histology.—The kidneys are entirely negative.

Rabbit 3L.—Weight, 2 pounds 1¼ ounces.

July 13. One-half c.c. urine culture of C. injected. Urine examined; microscopically negative; alkaline; albumin 0; cloudy, amorphous precipitate.

July 14. Urine examined; excess of pus cells; acid; albumin 0.

July 14, p. m. One-half c.c. reinjected.

July 15. Urine examined; excess of pus cells; acid; albumin +; weight, 1 pound 11¼ ounces.

July 15 to 17. Died.

Necropsy.—Much decomposed. Bladder urine filled with cellular, apparently epithelial, debris. Epithelial debris from both ureters. Gallbladder shows marked injection, and suppuration; portion of stomach at pyloric end adhering to it is hemorrhagic. Kidneys are large and bluish-brown in color. On section there are seen numerous yellow dots and lines in the medulla; marked degeneration of the cortex; numerous linear abscesses, extending to papilla in the medulla; intense congestion.

Histology.—There are innumerable abscesses in medulla.

Rabbit 4L.—Weight 2 pounds.

July 13, 3:30. One-quarter c.c. of urine culture of C. injected. Urine examined; microscopically negative; alkaline; albumin 0; cloudy, amorphous precipitate.

July 14. Microscopically negative; acid; albumin +.

July 14 p. m. One-quarter c.c. reinjected.

July 14 to 15. Died.

Necropsy.—On opening the peritoneum the descending colon for a distance of about 4 inches is of dark, reddish-brown color and considerably distended. There is a sharp transition at both ends to practically normal intestinal wall. On opening up the colon this region is seen to be markedly hemorrhagic and

somewhat thickened showing the same abrupt transition to normal tissue. The kidneys show a few small hemorrhages in the surfaces. The pelvis shows nothing abnormal.

Histology.—The kidneys are entirely negative.

Rabbit 2F.—Weight, 1 pound 15¾ ounces.

June 9. One c.c. of urinary culture of B. injected. Urine negative for albumin and pus cells.

June 10. Urine acid, cloudy with amorphous precipitate; no cells; albumin +.

June 12. Acid, cloudy, precipitate largely amorphous; some pus cells; many bacteria; albumin +.

June 14. Weight, 1 pound 12¼ ounces. Urine thick and stringy, full of masses and strings of amorphous material; acid; no cells; few bacteria; albumin ±.

June 15. Urine very cloudy; full of amorphous material; a few pus cells; albumin +.

June 16. Urine cloudy; much amorphous material; some pus cells; albumin ±.

June 17. Sacrificed.

Necropsy.—Findings were entirely negative; examination of bladder urine showed many pus cells as well as some amorphous material; urinary culture showed a gram-negative bacillus and gram-positive coccus.

Histology.—Kidney showed slight infiltration of a portion of the pelvis; marked cloudy swelling of parenchyma.

Rabbit 3F.—Weight, 1 pound 6 ounces.

June 9. One-half c.c. of urinary culture of B. injected. Urine negative for albumin and pus.

June 10. Urine slightly acid; brownish-yellow; cloudy with amorphous precipitate; few bacteria; no cells; albumin ++.

June 12. Acid urine; cloudy, amorphous precipitate and masses of shreds and debris of all kinds; albumin ++.

June 14. Weight, 1 pound 1¼ ounces. Urine very cloudy; full of pus cells and motile bacteria; albumin ++; acid.

June 15. Urine cloudy; full of pus cells; albumin ++.

June 16. Urine cloudy; full of pus cells; albumin +. Sacrificed.

Necropsy.—On opening the peritoneal cavity the serous surfaces are everywhere smooth. The bladder is distended with cloudy urine, the ureters are not distended; the kidneys are smooth on the surface but in two places on left and in one place on the right there is an opaque, yellowish area from 1 to 3 mm. in diameter. On section through areas they are seen to extend into the medulla in a long, yellowish streak practically to the papilla. The pelvis shows nothing unusual. The gallbladder is distended; outer surfaces are smooth, and contents consist of thick purulent material. Some coccidiosis of liver. The stomach, duodenum, appendix and cecum show nothing unusual. The pericardium adheres over the entire upper portion of the heart and is covered with a thick, creamy exudate. Culture from the bladder shows a gram-positive coccus and a gram-negative bacillus; also from the pelvis of the kidney and the gallbladder a gram-positive coccus and a gram-negative bacillus; from an abscess of the kidney a gram-positive coccus alone; from the heart, a gram-positive coccus alone.

Rabbit 4F.—Weight, 1 pound 4¾ ounces.

June 9. One c.c. of culture injected. Urine negative for albumin and pus.

June 10. Urine acid; pretty clear; slight amorphous precipitate, no cells or bacteria; albumin +.

June 12. Urine acid; cloudy, amorphous precipitate; no cells; few bacteria; albumin +.

June 14. Weight, 1 pound 3¾ ounces; urine very cloudy; stringy, amorphous masses; no cells; acid; albumin ±.

June 15. Urine cloudy; stringy substance present; few cells; acid; albumin +.

June 17. Sacrificed.

Necropsy.—Findings are entirely negative. Urine cloudy, with amorphous precipitate; no cells. Urine culture showed a gram-positive coccus and a gram-negative bacillus.

Histology.—Kidneys contain numerous pus cells in groups in the pelvis and in the lumen of the ureter. The bladder is negative.

Rabbit 3G.—Weight, 1 pound.

June 17. One c.c. of suspension of culture from kidney abscess of Rabbit 3F injected intravenously.

June 19. Found dead; ill the afternoon of June 18.

Necropsy.—On opening the peritoneum a portion of the ileum just above the ileocecal valve is found reddened and hemorrhagic. The most marked area is found about 1 foot above the ileocecal valve. This portion of the bowel on opening is studded with small hemorrhages, and on a portion of the wall there is a diphtheritic exudate. The appendix is thickened, and in an area about 1 inch below its attachment to the cecum is deeply injected and hemorrhagic and of an opaque, yellowish color. The appendix on opening shows in this hemorrhagic area a hemorrhagic exudate and considerable necrosis of the wall. The urine is cloudy, and on microscopic examination shows some casts and a few pus cells, and a considerable number of epithelial cells. The kidneys are much enlarged, opaque, of yellowish color, studded with groups of minute hemorrhages which give the kidney a mottled appearance. On section the hemorrhages are seen to be limited to the cortex and resemble the appearances on the outside. The heart is negative. A pure culture of a gram-negative bacillus was obtained from the submucosa of the appendix and from the bladder. The kidney cortex culture was negative.

Histology.—The kidney shows numerous hemorrhages in the cortex and considerable degeneration and necrosis of tubules. There are also some minute areas of infiltration in the cortex.

Rabbit 4G.—Weight, 1 pound 8¾ ounces.

June 19. One c.c. of culture from abscess of left kidney injected intravenously. Urine acid; negative.

June 20. A few cells; some amorphous material; slightly acid; no albumin.

June 21. Sacrificed.

Necropsy.—Peritoneum clear; appendix and cecum negative. Gallbladder hemorrhagic. The stomach has few small hemorrhages in the cardiac end; a small ulcer (?). The duodenum has six to eight hemorrhages just beyond the pyloric ring. The heart is negative. The kidneys are large, yellow and pale; cortex smooth but studded with minute hemorrhages over the entire surface; same in both kidneys. There are also small areas of more opaque, yellow appearance. The bladder shows numerous small submucous hemorrhages, one of somewhat larger size. Urine from the bladder shows albumin, epithelial cells, casts and leukocytes. Cultures of the urine are negative.

Histology.—The kidney cortex has no hemorrhages in the sections studied. There is marked degeneration and necrosis of epithelium in areas. The stomach and duodenum show hemorrhages in the mucosa.

Rabbit 7G.—June 20. One c.c. from abscess of left kidney, Rabbit 3F injected. Urine negative; acid.

June 21. Urine contains a few pus cells; acid; albumin +.

June 22. Urine acid; numerous pus cells; albumin +; diarrhea.

June 23. Urine acid; numerous pus cells, albumin +; diarrhea.

June 26. Diarrhea; urine contains numerous cells and groups of cells; albumin +.

June 27. Dying; chloroformed.

Necropsy.—On opening the abdomen the bladder is markedly distended with urine. The serous surfaces are everywhere smooth. The only unusual thing is a peculiar yellowish discoloration of that part of the ileum just above the ileocecal valve. The gallbladder is distended and filled with a thick yellowish material. On opening the chest the right ventricle of the heart is seen to be much dilated and of a yellowish color. The lungs are negative. The bladder shows a perfectly normal mucous membrane. There are no hemorrhages of the wall. The appendix is normal; the cecum is somewhat thickened near the ileocecal valve, and for a distance of about 6 inches above is somewhat thickened and in patches covered with a yellowish membrane firmly adhering to the mucous membrane. The stomach and doudenum show nothing unusual. The right kidney is of a brownish-red color and shows one or two lighter areas. On section it is of about normal thickness and the same color as the external surface. The medulla is somewhat edematous. There is pus in the pelvis of the kidney, but no hyperemia. The ureters and bladder are normal. On the left kidney are opaque yellowish areas which are limited to the cortex. The pelvis contains pus; otherwise nothing unusual. Cultures from the gallbladder and bladder contain a pure gram-negative bacillus.

Histology.—There is infiltration about many glomeruli. The pelvis of both kidneys shows an intact mucous membrane, but just below the epithelium there is a marked infiltration with leukocytes; also in the tips of the papillae. In the colon a diphtheritic membrane covers a large area of the surface. There is complete destruction of the mucosa and submucosa, and massive infiltration and fibrosis of the entire wall.

TWENTY-FOUR-HOUR METABOLISM OF TWO NORMAL INFANTS WITH SPECIAL REFERENCE TO THE TOTAL ENERGY REQUIREMENTS OF INFANTS *

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A series of investigations of the metabolism of normal infants were begun five years ago by Benedict and the writer at the Nutrition Laboratory of the Carnegie Institution of Washington with the object of obtaining a curve of the "basal" metabolism of normal infants. Some of these studies have already been published, and the rest are in the process of completion to be published later. Their primary object is to obtain the "basal" metabolism of infants (the metabolism at rest) for the purpose of comparing health with disease. The basal metabolism should mean that the subject is in complete muscular repose, and in the "postabsorptive" state, that is, when absorption of material from the alimentary tract has ceased. Since it is almost impossible to obtain a period of complete muscular repose in infants in the "postabsorptive" state and hungry, the term "basal" metabolism will be used in this communication in describing quiet periods shortly after food has been given. Since the results of these studies do not take into consideration the extra energy used up in muscular exercise, lost in the excreta or deposited in the body in the form of new tissue, they cannot be used as a definite measure of the food requirements of a normal growing infant. They contain information, however, which, with additional knowledge, helps in estimating the total caloric requirements of infants.

A careful review of the literature shows that there have been few instances in which an attempt has been made to obtain the twenty-four-hour metabolism of normal infants. The fundamental experiments of Rubner and Heubner[1] stand out as giving the only twenty-four-hour figures available for normal infants. They give records of three different normal infants weighing 5, 8 and 10 kg., the first and last being fed on human milk, and the second on a mixture of cow's milk. These infants were inside a respiratory chamber about twenty hours of the twenty-four-hour day. Unfortunately, complete records of the individual periods in these experiments showing the percentage increase in calories from rest to muscular activity are not available. Heubner, on

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1. Rubner and Heubner: Ztschr. f. biol., 1898, **36,** 1. Rubner and Heubner: Ztschr. f. biol., 1899, **38,** 315. Heubner: Berl. klin. Wchnschr., 1901, **38,** 449. Rubner and Heubner: Ztschr. f. exper. Path. u. Therap., 1905, **1,** 7.

the basis of these and other studies, maintains that an average normal infant requires per twenty-four hours, 100 calories per kilogram of body weight during the first three months of life, 90 calories during the second three months, and 80 or less calories during the last half of the first year of life. These figures are usually accepted as a basis from which to compute the energy requirements of normal infants.

The great difficulty of obtaining complete records of the respiratory metabolism for twenty-four hours accounts for the paucity of material reported above. The present investigation was carried on under Miss Alice Johnson and assistants, whose careful work and devotion day and night are responsible for the success of a very difficult piece of work, and without whose hearty cooperation it would have been impossible.

The purpose of the present investigation was to determine, if possible, how much extra energy was expended in the ordinary muscular activity of an infant during a twenty-four-hour day. It has been known for a long time that muscular activity increases the metabolism, but, on the other hand, there is no measure of how much of the day the infant is active. If the increase in metabolism due to muscular activity can be determined, if the factor of growth and the factor of energy lost in the excretions be established, this material could be used in conjunction with the average curve of the "basal" metabolism to estimate the number of calories in the food necessary for an infant in a twenty-four-hour day.*

The normal infants in the Directory for Wet-Nurses of the Boston Infants Hospital were selected for this purpose. The plan of the observation was to have the infant inside the respiratory chamber as many hours out of the twenty-four as possible so that an accurate measure of the total respiratory exchange could be obtained.

The periods were started at about 7 p. m., and run through the following twenty-four hours, stopping at the same time the next evening. Short periods were recorded so that it would be possible to select periods of absolute quiet as well as periods of activity. The cover was raised at regular intervals and the baby removed, nursed by his mother, and the diapers changed when soiled. It was due to the intelligent cooperation of the mothers that in one instance the infant was inside the respiratory chamber twenty-two hours and thirty-one minutes, and in the other, twenty-three hours and ten minutes. The flexibility of the apparatus made this possible without impairing the accuracy of the

* A tentative curve may be found in Morse and Talbot, Diseases of Nutrition and Infant Feeding, New York, 1915, p. 61. When such a curve is used the variations from the average should always be borne in mind, if it is applied to a single infant, because averages are made up from several subjects and the extremes may be as much as 10 per cent. one or the other side of the average figure.

results. The length of the actual observation compares very favorably with those of Rubner and Heubner, which were in all instances shorter.

E. L., girl, was born January 27, 1916, full term, the labor was normal and the baby weighed 3.71 kg. (8 pounds, 3 ounces) at birth. She was entirely breast fed up to date, receiving the breast every three hours. She had never been sick. Her weight April 20, 1916, was 5.03 kg. (about 11 pounds). The details of the twenty-four hours during which the respiratory exchange was measured are as follows:

	6:48 p. m.	—Nursed at breast
7:23 p. m. to	1:10 a. m.	—In respiratory chamber. Quieted down. Slept
1:10 a. m. to	1:25 a. m.	—Taken out, diapers changed. Nursed nine minutes. Returned to chamber
1:25 a. m. to	2:02 a. m.	—Restless
2:02 a. m. to	3:15 a. m.	—Sleeping
3:15 a. m. to	3:51 a. m.	—Moving about
3:51 a. m. to	4:30 a. m.	—Quiet
4:46 a. m. to	6:40 a. m.	—Moving and cried at intervals
6:40 a. m. to	6:54 a. m.	—Taken out, given breast, diapers changed, wet with urine. Returned to chamber
6:54 a. m. to	7:54 a. m.	—Played with hands and moved
7:54 a. m. to	8:39 a. m.	—Asleep
8:39 a. m. to	9:26 a. m.	—Moved hands and twisted body. Taken out, diapers wet, changed. Nursed. Returned to chamber
9:46 a. m. to	10:40 a. m.	—Moving and restless
10:40 a. m. to	11:14 a. m.	—Quiet
11:14 a. m. to	12:31 p. m.	—Grumbling, moving, waving hands, cooing
12:31 a. m. to	12:51 p. m.	—Taken out, given breast. Diaper soiled with small, brownish yellow stool. Returned to chamber
12:51 p. m. to	1:45 p. m.	—Gradually became quiet
1:45 p. m. to	3:00 p. m.	—Twisted, grumbled or played with hands
3:00 p. m. to	3:29 p. m.	—More restless
3:29 p. m. to	3:49 p. m.	—Taken out, diapers changed, nursed. Returned to chamber
3:49 p. m. to	7:23 p. m.	—Moderately active
	7:23 p. m.	—Taken out

She was weighed before and after each nursing and received amounts of breast milk as shown in Table 1.

TABLE 1.—Amounts of Breast Milk Received by Infant E. L. in Twenty-Four Hours

Date	Time	Grams	Ounces
4/20/16	7:07 p. m.	90	3
4/21/16	1:21 a. m.	135	4½
4/21/16	6:50 a. m.	135	4½
4/21/16	9:42 a. m.	145	4¾
4/21/16	12:48 p. m.	90	3
4/21/16	3:45 p. m.	100	3¼
Total in 24 hr.		695	23¼

TABLE 2.—RESULTS OF THE MEASUREMENTS OF GASEOUS METABOLISM OF INFANT E. L.

Period	Time	Length of Period, Min.	CO_2 Produced		Average Pulse Rate	Respiratory Quotient
			Measured, Gm.	Calculated to Hour Basis, Gm.		
Preliminary	7:23 – 7:53 p. m.	30	2.88	5.76	126	
1st	7:53 – 8:28 p. m.	35	2.46	4.22	117	0.92
2d	8:28 – 9:03 p. m.	35	2.58	4.42	119	0.94
3d	9:03 – 9:39 p. m.	36	2.52	4.20	118	0.88
4th	9:39 –10:14 p. m.	35	2.46	4.22	116	0.86
5th	10:14 –10:51 p. m.	37	2.71	4.39	112	0.91
6th	10:51 –11:27 p. m.	36	2.48	4.13	114	0.88
7th	11:27 p. m.–12:04 a. m.	37	2.31	3.75	115	0.80
8th	12:04 –12:38 a. m.	34	2.22	3.92	115	0.90
9th	12:38 – 1:10 a. m.	32	2.16	4.05	117	0.81
Preliminary	1:25 – 1:53 a. m.	28	2.80	6.00	132	
1st	1:53 – 2:32 a. m.	39	2.78	4.28	121	0.86
2d	2:32 – 3:09 a. m.	37	2.82	4.57	120	0.97
3d	3:09 – 3:58 a. m.	49	3.62	4.43	121	0.87
4th	3:58 – 4:49 a. m.	51	4.33	5.09	122	0.88
5th	4:49 – 5:39 a. m.	50	5.25	6.30	140	0.91
6th	5:39 – 6:15 a. m.	36	2.47	4.12	122	0.84
7th	6:15 – 6:40 a. m.	25	3.01	7.22	152	0.80
Preliminary	6:54 – 7:17 a. m.	23	2.50	6.52	145	
1st	7:17 – 7:56 a. m.	39	4.31	6.63	139	0.88
2d	7:56 – 8:31 a. m.	35	2.78	4.77	117	0.83
3d	8:31 – 9:26 a. m.	55	5.51	6.01	125	0.81
Preliminary	9:46 –10:04 a. m.	18	2.11	7.03	146	
1st	10:04 –10:32 a. m.	28	2.77	5.94	136	0.98
2d	10:32 –11:00 a. m.	28	1.92	4.11	115	0.86
3d	11:00 –11:33 a. m.	33	2.66	4.84	122	0.82
4th	11:33 a. m.–12:08 p. m.	35	3.87	6.63	143	0.90
5th	12:08 –12:31 p. m.	23	2.35	6.13	133	0.86
Preliminary	12:51 – 1:27 p. m.	36	2.87	4.78	119	
1st	1:27 – 2:16 p. m.	49	4.15	5.08	121	0.92
2d	2:16 – 3:29 p. m.	73	8.57	7.04	140	0.85
Preliminary	3:49 – 4:15 p. m.	26	2.84	6.55	128	
1st	4:15 – 4:47 p. m.	32	3.48	6.53	138	0.86
2d	4:47 – 5:14 p. m.	27	2.70	6.00	123	0.90
3d	5:14 – 6:19 p. m.	65	6.44	5.94	143	0.83
4th	6:19 – 6:52 p. m.	33	3.49	6.35	136	0.87
5th	6:52 – 7:23 p. m.	31	3.62	7.01	142	0.85
Total..........................		22 hr. 31 min.	120.80	....	...	0.87

The results of the measurements of the gaseous metabolism of E. L., aged 2 months, 3 weeks, weight 5.03 kg., for the twenty-four hours, April 20-21, 1916, are given in Table 2.

E. S., girl, was born at full term, Oct. 14, 1915. She weighed 6 pounds (2.72 kg.) at birth. She was always breast fed and did fairly well until February, 1916, when she had some indigestion and colic, and some facial eczema. These symptoms gradually straightened out, and on April 19, when 6 months and 1 week old, she weighed 5.76 kg. (the average weight for the age is 7.8). She finished nursing at 6:51 p. m., April 19, 1916. The program for the twenty-four-hour day was as follows:

6:51 p. m.	—Finished nursing
7:02 p. m. to 5:51 a. m.	—Placed in chamber. Quickly went to sleep. Occasional muscular movement recorded on smoked drum
5:52 a. m. to 6:08 a. m.	—Taken out, nursed, returned to chamber
6:08 a. m. to 8:13 a. m.	—Asleep
8:13 a. m. to 8:51 a. m.	—Moderate moves
8:56 a. m. to 9:08 a. m.	—Taken out, nursed, returned to chamber
9:08 a. m. to 10:15 a. m.	—Cooed, kicked, played, smiled, occasionally cried
10:15 a. m. to 12:14 p. m.	—Quiet, very few moves
12:14 p. m. to 12:46 p. m.	—More active
12:46 p. m. to 12:57 p. m.	—Taken out, nursed, diapers changed, returned to chamber.
12:57 p. m. to 2:08 p. m.	—Kicking and waving hands
2:08 p. m. to 2:51 p. m.	—Asleep
2:51 p. m. to 3:48 p. m.	—Active, crying or laughing
3:48 p. m. to 4:00 p. m.	—Taken out, nursed, diapers changed, returned to chamber
4:00 p. m. to 5:19 p. m.	—Played, moved and wiggled
5:19 p. m. to 7:03 p. m.	—Asleep with the exception of a few minutes of play

She was weighed before and after each nursing and received amounts of breast milk as shown in Table 3.

TABLE 3.—Amounts of Breast Milk Received by E. S. in Twenty-Four Hours

Date	Time	Grams	Ounces
4/19/16	6:51 p. m.	70	2¼
4/20/16	5:56 a. m.	135	4½
4/20/16	9:07 a. m.	125	4¼
4/20/16	12:54 p. m.	150	5
4/20/16	3:57 p. m.	135	4½
Total in 24 hr.		615	20½

The results of the measurements of the gaseous metabolism of E. S., aged 6 months, 1 week, weight 5.76 kg., for twenty-four hours, April 19-20, 1916, are given in Table 4.

TABLE 4.—RESULTS OF THE MEASUREMENTS OF GASEOUS METABOLISM OF INFANT E. S.

Period	Time	Length of Period, Min.	CO_2 Produced		Average Pulse Rate	Respiratory Quotient
			Measured, Gm.	Calculated to Hour Basis, Gm.		
	April 19					
Preliminary	7:02 – 7:23 p. m.	21	1.99	5.69	135	
1st	7:23 – 7:59 p. m.	36	2.76	4.60	120	0.83
2d	7:59 – 8:34 p. m.	35	2.87	4.92	129	0.81
3d	8:34 – 9:04 p. m.	30	2.46	4.92	121	0.81
4th	9:04 – 9:36 p. m.	32	2.75	5.16	130	0.82
5th	9:36 – 9:44 p. m.	8	0.61	4.58	127	
2d Prelim.	9:44 –10:03 p. m.	19	1.59	5.02	129	
1st	10:03 –10:37 p. m.	34	2.73	4.82	128	0.81
2d	10:37 –11:07 p. m.	30	2.23	4.46	129	0.85
3d	11:07 –11:38 p. m.	31	2.33	4.51	130	0.80
4th	11:38 p. m. 12:15 a. m.	37	3.12	5.06	130	0.87
	April 20					
5th	12:15 –12:50 a. m.	35	2.83	4.85	130	0.88
6th	12:50 – 1:22 a. m.	32	2.79	5.23	136	0.86
7th	1:22 – 1:59 a. m.	37	2.87	4.65	126	0.84
8th	1:59 – 2:32 a. m.	33	2.77	5.04	139	0.85
9th	2:32 – 3:24 a. m.	52	5.07	5.85	136	0.79
10th	3:24 – 3:58 a. m.	34	2.62	4.62	141	0.88
11th	3:58 – 4:27 a. m.	29	2.68	5.54	143	0.85
12th	4:27 – 5:16 a. m.	49	4.74	5.80	146	0.84
13th	5:16 – 5:52 a. m.	36	3.67	6.12	154	0.79
Preliminary	6:08 – 6:28 a. m.	20	2.21	6.63	153	
1st	6:28 – 7:01 a. m.	33	2.88	5.24	137	0.84
2d	7:01 – 7:50 a. m.	49	4.49	5.50	131	0.85
3d	7:50 – 8:19 a. m.	29	2.53	5.23	118	0.84
4th	8:19 – 8:56 a. m.	37	3.64	5.90	124	0.80
Preliminary	9:08 –10:07 a. m.	59	7.64	7.77	151	
1st	10:07 –10:34 a. m.	27	1.87	4.16	120	0.79
2d	10:34 –11:05 a. m.	31	2.85	5.52	122	0.88
3d	11:05 –11:32 a. m.	27	2.05	4.56	119	0.79
4th	11:32 a. m. 12:02 p. m.	30	2.76	5.52	130	0.81
5th	12:02 –12:28 p. m.	26	2.05	4.73	118	0.78
6th	12:28 –12:46 p. m.	18	1.92	6.40	148	0.89
Preliminary	12:57 – 2:12 p. m.	75	8.90	7.12	142	
Preliminary	2:12 – 3:48 p. m.	96	10.19	6.37	137	
Preliminary	4:00 – 4:22 p. m.	22	2.80	7.64	135	
1st	4:22 – 4:54 p. m.	32	4.26	7.99	148	0.85
2d	4:54 – 5:25 p. m.	31	3.80	7.35	142	0.81
3d	5:25 – 5:56 p. m.	31	2.40	4.65	114	0.76
4th	5:56 – 6:36 p. m.	40	3.64	5.46	126	0.79
5th	6:36 – 7:03 p. m.	27	2.08	4.62	122	1.02
Total..........................		23 hr. 10 min.	130.44	....	...	0.83

An average of the figures of the "basal" and of the maximum metabolism of E. L. are given in Table 5.

TABLE 5.—AVERAGE OF THE "BASAL" AND MAXIMUM METABOLISM OF INFANT E. L.

	No. of Periods	Carbon Dioxid, Gm. per Hr., Average	Heat Computed (24 hr.) Calories			Average Pulse
			Total	Per Kg.	Per Sq. M. Lissauer	
"Basal" metabolism..............	12	4.15	285	57	944	117
Maximum metabolism............	20	6.24	428	85	1417	135

The "basal" metabolism of 285 calories was increased 143 calories by muscular activity. This corresponds to an increase of 67 per cent.

The average figures of the "basal" and of the maximum metabolism of E. S. are given in Table 6.

TABLE 6.—AVERAGE OF THE "BASAL" AND MAXIMUM METABOLISM OF INFANT E. S.

	No. of Periods	Carbon Dioxid, Gm. per Hr., Average	Heat Computed (24 hr.) Calories			Average Pulse
			Total	Per Kg.	Per Sq. M. Lissauer	
"Basal" metabolism..............	18	4.75	338	59	1021	126
Maximum metabolism............	12	6.75	481	84	1453	143

The "basal" metabolism of E. S. was increased 143 calories by muscular activity which corresponds to an increase of 70 per cent. This is very close to the average increase of 65 per cent. found in the new-born infant.[2]

Since the infants were removed from the chamber at regular intervals during the twenty-four hours for their usual nursings, the metabolism obviously could not be measured during that time, but an estimate of what it would have been is justifiable. Considerable muscular work is performed in nursing, and if the average maximum metabolism for each infant is taken to represent the metabolism during that time, it cannot be far from the truth. Baby E. L. was out of the chamber one hour and twenty-nine minutes, and Baby E. S., fifty minutes. The estimated metabolism for fifty minutes for Baby E. S. would be found as follows:

2. Benedict and Talbot: Physiology of the New-Born Infant, Carnegie Institution of Washington, Publication 233, p. 112, Table 17.

The average maximum total metabolism is 481 calories; divide this by twenty-four hours and it will give 20 calories, the amount produced in one hour; 50/60 of 20 = 17 calories, or the amount theoretically excreted during the fifty minutes that E. S. was out of the chamber.

Tables 7 and 8 give the total number of calories used up by Infants E. L. and E. S.

TABLE 7.—Total Number of Calories Used by Infant E. L.

Period	Carbon Dioxid, Gm.	Respiratory Quotient	Heat Computed (24 hr.) Calories			Pulse Rate
			Total	Per Kg.	Per Sq. M. Lissauer	
Measured 22 hr., 31 min.	120.8	0.87	345	..	....	127
Estimated 1 hr., 29 min.	9.3	....	27			
Total	130	....	372	74	1232	

TABLE 8.—Total Number of Calories Used by Infant E. S.

Period	Carbon Dioxid, Gm.	Respiratory Quotient	Heat Computed (24 hr.) Calories			Pulse Rate
			Total	Per Kg.	Per Sq. M. Lissauer	
Measured 23 hr., 10 min.	130.4	0.83	387	..	....	127
Estimated 50 min.	5.6	....	17			
Total	136.0	....	404	70	1232	

What is measured is the actual heat produced by these infants. There are, however, other ways in which energy may be lost from the body, such as the potential energy of the urine and feces. This energy which is lost must be supplied in the food. An estimate of this loss is, of course, open to many objections, and the figure given here will be modified by future investigations. Presumably the greatest single factor to take into consideration is the fat lost in the feces, which with the urea in the urine should not exceed 15 per cent. of the total measured metabolism in a normal infant.

When the factor for the food lost in the excreta has been added to the total, and that amount of food given to the infant, it should neither gain nor loose weight, but should remain in an equilibrium. Extra food must, therefore, be added so that the baby may grow. This figure is also difficult to estimate. Clinically, when infants are receiving only slightly more food than is necessary to maintain an equilibrium, they

gain very slowly in weight, whereas, if they are given more food they gain more rapidly. Rubner and Heubner's infants received a little less than 15 per cent. of the total measured calories for growth. If 20 per cent. is taken for the growth factor, it should give enough leeway for the infants to gain.

A rough estimate of the caloric requirements of a normal infant may be made by adding the calories used up by muscular activity to the basal metabolism. If the infant is very quiet, 15 per cent. should be added, if normally active 25 per cent., and if extremely active, about 40 per cent. To the result add 15 per cent. for energy lost in the excreta and 20 per cent. for growth. In the case of E. L. we know how many calories were actually used up in muscular exercise. Therefore, all that is necessary is to add the probable number of calories necessary to allow for growth and what is lost in the excreta. If 35 per cent. is added to the 74 calories per kilogram of body weight actually used by E. L., it is found that she needs about 100 calories per kilogram of body weight in her food. If the same thing is done for E. S., the food requirements are found to be about 94 calories per kilogram of body weight.

It is probable that infants fed on cow's milk, particularly on formulas containing large amounts of protein, will require even more food than infants fed on human milk, because the stimulating action of protein causes extra heat to be burned during digestion. The caloric requirements of normal infants obviously are not the same as those of the sick infant whose "basal" metabolism is higher per kilogram of body weight and who may use up additional energy because of increased restlessness from colic or discomfort, burn it up in fever, or may not absorb all the food given him, as happened in one infant who lost 20 per cent. of the food calories in the feces. Neither does it apply to the infant with a subnormal temperature, indicating depressed vital functions. These infants come under another category and require further study to answer many of the points now obscure.

SOME ANALYSES OF VEGETABLES SHOWING THE EFFECT OF THE METHOD OF COOKING *

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The addition of green vegetables to the dietary of young infants is becoming a common practice. It is generally believed that the value of this is due to the effect on the mineral metabolism. Infants who are fed for too long a time on an exclusive milk diet show anemia, late closure of the fontanel, delay in walking and general lack of activity. The secondary anemia is easily explained by the small amount of iron in cow's milk; after its dilution in milk formulas the amount of iron becomes almost negligible. Instead of making use of drugs to supply the needed iron, green vegetables have been fed to many children in the wards and the outpatient department of the Babies' Hospital. This plan has been followed with children as young as 6 or 7 months. It has been interesting to observe that infants thus fed show an earlier closure of the fontanel and generally greater activity than those without such additions to their diet.

How this beneficial effect is produced is a nutritional problem which is not within the scope of this paper. It has been variously explained. The mere addition of an increased quantity of salts may be advantageous. The particular combinations of the bases with the inorganic and organic acids present may provide the salts in an especially suitable form for use by the organism. A third view is that the value of the vegetables lies in a biologic or so-called vitamin effect. Since the general opinion is that the mineral content is the important factor, we have studied the subject from this point of view. We hoped to shed a little light on the question by determining the mineral metabolism of infants suffering with rickets and those showing delayed development, comparing their salt retention with and without vegetable additions to the diet.

The question immediately arose as to what was the actual mineral content of the vegetables as ordinarily prepared and administered.

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* From the Laboratories of the Rockefeller Institute for Medical Research and the Babies' Hospital.

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Abundant figures are available which show the total mineral content of the edible part of various vegetables. It is obvious, however, that the water used in cooking extracts more or less of the constituents and it is not a common practice to give this with the vegetable. Hence it is evident that the reported analyses are of no value in estimating the mineral content of vegetable additions to the diet of children. We therefore undertook a series of analyses of cooked vegetables, considering separately the solid portion ordinarily given as food and the water used in cooking.

At first the vegetables were cooked in the manner usual when preparing them as food for children; that is, by a very thorough boiling. After cooking, the vegetables were drained in a colander and the resulting solids and water were analyzed separately. The figures here reported are computed on the basis of 100 gm. of the edible portion of the uncooked vegetable (approximately a quarter of a pound).

TABLE 1.—Content in Grams of Solids of Vegetables Prepared by Boiling

Vegetable	Minutes Boiled	Solids	Ash	CaO	MgO	P_2O_5	Cl	K_2O	Na_2O	H_2SO_4	Fe_2O_3	Total N	N. as Protein
Spinach	90	8.30	1.172	0.305	0.035	0.123	0.036	0.238	0.068	0.034	0.0090	0.497	3.10
New Zealand spinach	30	4.26	0.535	0.145	0.021	0.062	0.000	0.157	0.040	0.016	0.0154	0.236	1.48
Young carrots	30	6.31	0.408	0.039	0.014	0.043	0.023	0.181	0.038	0.022	0.0070	0.108	0.67
Onions	45	6.82	0.398	0.020	0.013	0.067	0.008	0.186	0.010	0.056	0.0026	0.189	1.18
String beans	150	5.31	0.371	0.070	0.030	0.063	0.045	0.123	0.011	.....	......	0.190	1.19
Asparagus	30	4.59	0.370	0.038	0.021	0.101	0.024	0.174	0.001	0.025	Trace	0.283	1.77
Potatoes	30	20.51	.....	.....	.....	.....	.....	.....	.....	.....	......	.....	....

Table 1 shows the analyses of the solid portion of various vegetables boiled as described above.

Spinach shows the highest total salts, containing from two to three times as much ash as any of the other vegetables studied. This preponderance is due largely to calcium and phosphorus. The iron is highest in the New Zealand spinach, the ordinary spinach and carrots being next. The iron in onions is very low, while asparagus has only a trace. This table plainly shows that spinach is the most efficacious in supplying mineral addition.

New Zealand spinach is a comparative newcomer in the market. It does not belong to the same family as the ordinary spinach. It possesses the advantage of being available for a continuous supply throughout the summer, when ordinary spinach is not easily available. Although there is considerable waste in the preparation of New

Zealand spinach and it is rather a watery vegetable, it serves as a very satisfactory substitute for common spinach.

The analyses of the water drained from the cooked vegetables show very striking results. These are given in Table 2.

The excessive waste of salts if this water is discarded is very evident. It ranges from over a quarter of the total ash of onions to nearly

TABLE 2.—Percentage Lost in Water Under Ordinary Boiling Conditions

Vegetable	Minutes Boiled	Solids	Ash	CaO	MgO	P_2O_5	Cl	K_2O	Na_2O	H_2SO_4	Fe_2O_3	Total N
Spinach	90	32.2	45.2	Trace	61.5	48.2	71.1	64.8	61.1	57.2	28.2	23.1
New Zealand spinach	30	41.3	72.2	3.6	81.0	70.2	100.0	81.9	77.8	78.7	50.8	22.3
Young carrots	30	37.5	47.8	28.4	41.6	34.6	57.1	47.3	48.8	49.9	Trace	22.2
Onions	45	22.5	28.0	26.1	10.6	24.6	31.4	29.2	0	31.6	Trace	19.8
String beans	150	31.8	43.4	21.4	54.1	42.7	46.8	55.2	56.3	......	.....	26.7
Asparagus	30	27.4	46.7	26.6	40.1	34.6	46.4	49.2	Trace	52.1	Trace	24.1
Potatoes	30	4.4	.....	.....	.....	.....	.....	.....	.....	......	.....	....

three quarters of that of New Zealand spinach. In the others the loss is about half the total. Calcium is the only constituent which is not seriously affected. The examination of potatoes showed so small a loss of total solids that the analyses were not carried through.

An attempt was next made to reduce the loss by boiling the vegetables for minimum time. A comparison of the effect of long and short boiling is given in Table 3.

TABLE 3.—Comparison of Percentage Lost in Water with Long and Short Boiling

Vegetable	Minutes Boiled	Solids	Ash	CaO	MgO	P_2O_5	Cl	K_2O	Na_2O	H_2SO_4	Fe_2O_3	Total N
Spinach	90	32.2	45.2	Trace	61.5	48.2	71.1	64.8	61.1	57.2	28.2	23.1
Spinach	10	26.7	42.2	Trace	55.8	43.3	66.9	58.1	55.7	39.3	23.4	19.2
Beans	150	31.8	43.4	21.4	54.1	42.7	46.8	55.2	56.3	......	.....	26.7
Beans	60	28.2	39.4	12.2	43.3	40.9	25.4	53.9	44.1	......	.....	22.2

This table shows that the saving of salts by shorter boiling was insignificant. The only exceptions to this were the calcium and chlorid in the beans and the sulphate in spinach. Apparently the salts are lost early in the process of boiling.

Some modification of the method of cooking seemed to be necessary. Steaming was therefore tried, because it affords a method in

which the vegetables are held apart from the boiling water instead of soaking in it as in boiling. For this purpose a rice steamer was used. The vegetables are held in a tightly covered receptacle with a rather finely perforated bottom. This part fits closely on the top of the boiler which holds the water. Any type of steamer which holds the vegetables out of the water would undoubtedly serve as well.

Table 4 shows the results obtained by cooking the vegetables in this way.

TABLE 4.—Comparison of Percentage Lost in Water by Steaming and by Boiling

Vegetable	Method of Cooking	Minutes Cooked	Solids	Ash	CaO	MgO	P_2O_5	Cl	K_2O	Na_2O	H_2SO_4	Fe_2O_3	Total N
Spinach..........	Boiling...	10	26.7	42.2	Trace	55.8	43.3	66.9	58.1	55.7	39.3	23.4	19.2
Spinach..........	Steaming.	15	17.5	25.5	(a)	(a)	19.7	(a)	34.8	51.2	(a)	(a)	(a)
New Zealand spinach........	Boiling...	30	41.3	22.2	3.6	81.0	70.2	100.0	81.9	77.8	78.7	50.8	22.3
New Zealand spinach (b)....	Steaming.	30	5.2	15.3	7.9	22.3	29.8	7.3	19.4	50.5	21.3	0	0
Young carrots...	Boiling...	30	37.5	47.8	28.4	41.6	34.6	57.1	47.3	48.8	49.9	Trace	22.2
Young carrots...	Steaming.	15	8.8	13.6	(a)	(a)	10.7	(a)	10.0	14.3	(a)	Trace	(a)
Onions...........	Boiling...	45	22.5	28.0	26.1	10.6	24.6	31.4	29.2	0	31.6	Trace	19.8
Onions...........	Steaming.	30	20.4	25.5	27.9	7.9	21.6	28.2	26.6	0	23.2	Trace	18.7
Asparagus.......	Boiling...	30	27.4	46.7	26.6	40.1	34.6	46.4	49.2	Trace	52.1	Trace	24.1
Asparagus.......	Steaming.	30	8.5	15.2	(a)	(a)	11.5	(a)	15.8	0	(a)	(a)	(a)
Potatoes.........	Boiling...	30	4.4	.....	.....	.....	.....	.....	.....	.....	......	.....	....
Potatoes.........	Steaming	30	1.6	.....	.....	.....	.....	.....	.....	.....	......	.....	....

(a) The amount of solids in the water from the steamed vegetables was too small to permit making all determinations.
(b) An analysis of the water from the steamed New Zealand spinach was not made. The percentages lost were estimated by assuming the total content of the water and the solid portion to be the same in the steamed as in the boiled.

It is obvious from an examination of Table 4 that steaming is by far the most economical method of cooking for preserving the salts. The remarkable saving of salts should be emphasized. In spinach the loss by steaming becomes about half what it was in boiling. In asparagus it is less than a third, and in carrots it is not even a fourth. The effect of steaming on the different constituents of the New Zealand spinach is more variable than in case of the other vegetables. Sodium is lost in a high degree even in steaming, but the saving in the other constituents, except calcium, is very striking. Onions, which lost the least in boiling, were the least affected by the changed method of cooking. It is a strange fact that there is a slightly greater loss of calcium by steaming than by boiling, but since the calcium loss is small in any case, this is of little importance.

For the benefit of those who may wish to feed the vegetables steamed, Table 5 is presented.

As in Table 1, the figures in Table 5 are computed on the basis of 100 gm. of the edible portion of the uncooked vegetable. When cooked, this amount yields approximately three tablespoonfuls of all but carrots, which furnish four.

TABLE 5.—CONTENT IN GRAMS OF SOLIDS OF VEGETABLES PREPARED BY STEAMING

Vegetable	Minutes St'm'd	Solids	Ash	CaO	MgO	P_2O_5	Cl	K_2O	Na_2O	H_2SO_4	Fe_2O_3	Total N	N. as Protein
Spinach (c)..........	15	7.12	1.047	0.100	0.089	0.079	0.032	0.341	0.047	0.052	0.041	0.421	2.63
New Zealand spinach	30	6.88	1.628	0.139	0.085	0.124	0.009	0.701	0.090	0.059	0.037	0.305	1.91
Young carrots.......	15	9.50	0.669	0.047	0.025	0.063	0.047	0.276	0.074	0.019	0.014	0.137	0.86
Onions..............	30	6.70	0.402	0.019	0.016	0.070	0.010	0.195	0.012	0.057	0.003	0.199	1.24
Asparagus...........	30	5.93	0.556	0.030	0.026	0.145	0.040	0.285	0.001	0.039	Trace	0.373	2.33
Potatoes............	30	22.82	.....	.....	.....	.....	.....	.....	.....	.....	.....	.....	....

(c) The spinach given here was a different variety from that used for the boiling experiment. This kind had thick, curly, dark green leaves and its toal mineral content was much lower.

A comparison of Tables 1 and 5 makes impressive the greater concentration in salts of vegetables prepared by steaming. For example, from the same amount of New Zealand spinach one can obtain approximately three times as much mineral matter by steaming as is available by boiling.

A table follows (Table 6) in which the approximate content of one tablespoonful of spinach and of carrots, cooked by steaming, has been estimated from Table 5.

TABLE 6.—APPROXIMATE CONTENT OF ONE TABLESPOONFUL OF STEAMED VEGETABLE

Vegetable	Solids	Ash	CaO	MgO	P_2O_5	Cl	K_2O	Na_2O	H_2SO_4	Fe_2O_3	Total N	N. as Protein
Spinach......................	2.37	0.349	0.033	0.030	0.026	0.011	0.114	0.016	0.017	0.014	0.140	0.88
Young-carrots...............	2.40	0.167	0.012	0.006	0.016	0.012	0.069	0.018	0.005	0.004	0.034	0.21

If a steamer is not available, the cooking may be done in a double boiler. The vegetable should be prepared as usual, drained after washing and placed with no additional water in the inner boiler. Spinach requires about thirty minutes to cook in this manner. Table 7 gives a comparison of the result of this method of cooking with that by steaming.

It will be seen that there is very little choice between the two methods as regards the saving of salts.

TABLE 7.—COMPARISON OF SPINACH STEAMED AND THAT COOKED IN DOUBLE BOILER

	Method of Cooking	Solids	Ash	CaO	MgO	P_2O_5	Cl	K_2O	Na_2O	H_2SO_4	Fe_2O_3	Total N	N. as Protein
Content of solid portion from 100 gm. of spinach	Steaming	7.12	1.047	0.100	0.089	0.079	0.032	0.341	0.047	0.052	0.041	0.421	2.63
	Double boiler	8.03	0.997	0.166	0.049	0.107	0.024	0.243	0.114	.....	.....	0.574	3.59
Percentage lost in water of cooking	Steaming	17.5	25.5	(a)	(a)	19.7	(a)	34.8	51.2	(a)	(a)	(a)	....
	Double boiler	15.5	25.6	4.5	33.3	25.6	(a)	34.7	30.3	(a)	30.8	(a)	....

(a) The amount of solids in the water was too small to permit making all determinations.

Early in the paper reference was made to the possible importance of the combinations of bases with inorganic and organic acids. A study of the tables shows a great preponderance of bases over inorganic acids. This must mean that a considerable proportion of the bases are held as salts of organic acids. It is generally believed that such compounds are more assimilable than inorganic salts. Hence there would appear to be some ground for the theory that the beneficial effect of vegetable feeding is at least partly due to the character of the combinations of bases and acids.

Some metabolism experiments on the effect of vegetable addition to the food on the mineral balance are under way. With one child, somewhat rachitic and very backward in development, an improved balance was obtained after spinach had been added to a food otherwise considerably reduced. We hope to report these results, with those from other observations, later.

The methods used in obtaining the results reported in this paper are those previously used in work reported from these laboratories.[1] The iron was determined gravimetrically as iron phosphate.

CONCLUSIONS

1. A large proportion of the mineral content of most vegetables is lost in the water used in cooking by boiling.

2. This loss is only slightly reduced by making the time of boiling a minimum.

3. A very great saving in mineral content may be effected by using the method of steaming.

4. Spinach is the best vegetable to provide a salt addition to the diet.

Fifty-Fifth Street and Lexington Avenue.

1. Holt, L. E., Courtney, A. M., and Fales, H.: Chemical Composition of Diarrheal as Compared with Normal Stools in Infants, AM. JOUR. DIS. CHILD., 1915, **9,** 213.

ENLARGEMENT OF THE THYMUS TREATED BY THE ROENTGEN RAY *

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The purpose of this paper is to emphasize again three distinct facts with reference to enlargement of the thymus: (1) The condition is much commoner than is ordinarily supposed. (2) The diagnosis can be made definitely by means of simple physical examination and the Roentgen ray. (3) In the Roentgen ray we possess a therapeutic agent, which, in and of itself, will effect a cure in the vast majority of cases.

1. *Occurrence.*—According to some clinicians, enlargement of the thymus is supposed to be a rather rare condition. Those of us who have been particularly interested in the condition have been able to prove the fallacy of this view. The condition is in reality quite common. It is rather astonishing to note how frequently it is to be found if it be systematically searched for. As illustration of this I may refer to the paper of Dr. J. E. Benjamin, read before the Academy of Medicine of Cincinnati and now in press. In his individual service in the children's out-patient clinic (University of Cincinnati), Dr. Benjamin had 225 new cases in a year's time. Of these, nineteen showed indisputable evidence of enlarged thymus (8.4 per cent.). No other physician in the out-patient department found so many cases, because no other physician examined his patients so carefully with reference to this particular condition.

While very little is known about the etiology of enlarged thymus, certain facts have recently come to light in our studies. Quite a few of our cases have occurred in babies suffering from congenital syphilis. At present no conclusions can be drawn from this observation.

A distinct familial tendency has also been noted. In our recent cases four families had more than one child affected. Two pairs of twins came under observation, all four of the infants having enlarged thymus.

We have also noted an apparent relationship of hypertrophic stenosis of the pylorus and enlarged thymus. Dr. Dudley W. Palmer has recently reported a series of fourteen cases of congenital pyloric stenosis, of which seven had enlarged thymus. I have seen two additional cases occurring in the practice of Dr. Rachford.

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2. *Diagnosis.*—At the onset it should be borne in mind that some cases of enlarged thymus run a symptomless course. These latent cases are discovered only as the result of careful routine examination. Sudden death as the result of trauma, anesthesia or intercurrent affection occurs not infrequently in these cases. As a matter of fact, intercurrent affections frequently light up pressure effects of an enlarged thymus hitherto unsuspected. Thus, in a former paper I referred to a child, who had apparently been perfectly normal, brought to the hospital with typical thymic asthma after a severe attack of whooping-cough. Postmortem, a hyperplastic thymus was found.

Figure 1

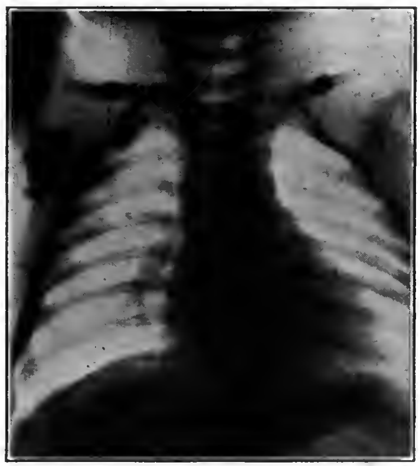

Figure 1a

Fig. 1.—F. E. before treatment, 3/12/17.
Fig. 1a.—F. E. after three treatments, 3/29/17.

There are three definite symptoms of enlarged thymus which are present singly or together. These are dyspnea, continuous or remittent, suffocative attacks, with cyanosis and stridor.

The dyspnea may be either permanent or intermittent. The permanent type is the more common. The respiratory difficulty increases until the child has a suffocative attack, accompanied by intense cyanosis. The attacks are repeated with greater or less frequency, and death may occur during one of them. Between attacks the dyspnea is continuous.

In the intermittent forms, children apparently quite normal and usually several months of age, are suddenly seized with suffocative attacks, accompanied by cyanosis — usually associated with convulsive movements of the extremities — followed after a few moments by a

return to an apparently normal state. The intervals between the attacks, at first considerable, tend to become constantly shorter. Variations and gradations of the two forms are common. Nocturnal cough, usually dry and hacking, is a frequent symptom in both forms.

Stridor, when present, is usually inspiratory. The frequent association of enlarged thymus and congenital stridor does not admit of question. But not all cases of congenital stridor are due to enlarged thymus, as was supposed by Hochsinger. Reflund and Koplik have shown that some cases are due to malformation of the epiglottis, and Lees and Thomson point out that in some cases the stridor is due to incoordination of the vocal cords, the result of muscular imbalance.

The diagnostic physical signs of greatest importance are these: Detection of a bulging mass in the jugulum (more often absent than present); enlargement of the area of normal thymus dulness on per-

Figure 2

Figure 2a

Fig. 2.—McN. before treatment, 3/25/17.
Fig. 2a.—McN. after three treatments, 4/17/17.

cussion. In young children there is a definite form of thymus dulness in the shape of an irregular triangle or truncated cone whose base is the sternoclavicular junction and whose apex is the second rib. Laterally, the dulness extends but very slightly beyond the sternum. Dulness beyond the sternal margins, especially dulness continuous with the area of heart dulness, is always very suggestive of enlarged thymus. The percussion of the area of thymic dulness is not difficult if one uses very light, or, at times, threshhold percussion. The claim of Boggs that the thymus dulness is movable, depending on whether the neck is flexed or extended, we have not been able to substantiate.

Definite information as to the existence of the enlargement of the thymus is afforded by the Roentgen ray. Certain requirements in the taking of these pictures must, however, be met. Dr. Sidney Lange of

Cincinnati has worked out a very careful technic. His procedure is here quoted in detail.

The child to be radiographed must be placed flat on the back. There must be no tilting to either side. If there is the slightest lateral tilting there is produced on the Roentgen-ray plate an asymmetry of the two halves of the chest and a "flopping" or displacement of the mediastinal and heart shadows to one or the other side. Roentgen-ray plates produced under such conditions are usually valueless, as they can not be accurately interpreted. It is not always easy to place very young infants symmetrically on their backs, but repeated trials must be made until a plate is produced which shows the chest areas, that is, the distances from the midline of the spine to axillary borders of the ribs, to be equal on right and left sides. Under these conditions, enlargements of the upper mediastinal shadow, whether to the right or to the left of the midline, can be readily recognized.

It is essential in the making of these roentgenograms of very young children that the exposure be almost instantaneous. The reasons are obvious.

Figure 3

Figure 3a

Fig. 3.—E. H. before treatment, 1/19/17.
Fig. 3a.—E. H. after three treatments, 2/6/17.

In the series here presented the time of exposure varied from one-sixtieth to one-thirtieth of a second. Even with such short exposures it is not always possible to secure absolutely sharp contours on the plates. If the time exceeds one-thirtieth of a second there results an amount of blurring.

A very soft Roentgen-ray tube should be used for this work, as the delicate thymus tissue will fail to cast a shadow on the Roentgen-ray plate if the quality of the Roentgen ray employed be too hard or penetrating.

The normal Roentgen-ray shadow is a median one, which normally rests on and is continuous with the heart shadow. Marked enlargement of this shadow, especially marked lateral enlargement, is characteristic of hypertrophied thymus. There is no difficulty, as a rule, in differentiating the shadow produced by enlarged thymus from that produced by congenital heart lesions or caseous lymph nodes. In a careful study of the interpretation of the thorax roentgenogram in the nursling, Benjamin and Goett point out that a broadening of the

shadow to the right may at times be due to large vessels, especially the vena cava superior. But, as they note, this cannot hold good when the larger part of the shadow falls to the left of the vertebral column.

In our work there has been no difficulty in eliminating this source of error in diagnosis.

Enlarged bronchial glands give an extra median shadow separate from the heart shadow and not connected with it. Ferrand, and Chatelin and Myer have also called attention to this point.

It would appear certain that enlargement of the thymus may exist, without the coexistence of the constitutional syndrome described by Paltauf as status lymphaticus.

This has been demonstrated repeatedly in our studies and is of importance, because children with enlarged thymus treated with the Roentgen ray get well and remain well, showing no further constitutional abnormality.

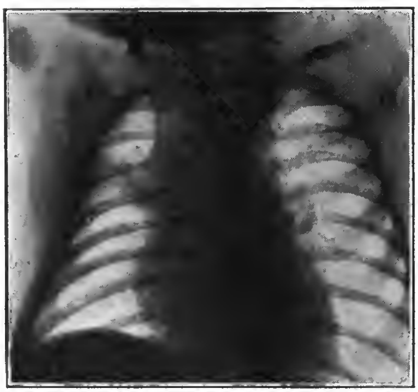

Figure 4

Figure 4a

Fig. 4.—O. before treatment, 11/9/16.
Fig. 4a.—O. after three treatments, 11/28/16.

Finally, with reference to diagnosis, it should be said that in doubtful cases where symptoms of thymic asthma appear without clearly demonstrable physical signs, the Roentgen-ray treatment given as a therapeutic test will often clear the diagnosis.

3. *Treatment.* — The treatment of enlarged thymus is in reality remarkably simple. The results of thymectomy may aptly be summarized in one sentence quoted from one of its advocates (Parker). Of the fifty patients operated on, seventeen died, a mortality of 33⅓ per cent. In the Roentgen ray we have a therapeutic agent at once safe and remarkably efficacious. Our series in Cincinnati now exceeds 100 cases, with four deaths.

The technic of the treatment as worked out by Lange is as follows: A Coolidge tube, backing up a 9½-inch spark, was employed. The rays were filtered through 4 mm. of aluminum and a piece of thick leather. The target skin distance was approximately 9 inches. The routine exposure was 25 milliampereminutes. In mild cases a single dose given over the anterior surface of the chest proved sufficient. In more urgent cases 50 milliampereminutes were administered at the first treatment, 25 anteriorly and 25 posteriorly. During the treatment the child was kept quiet by four sandbags, one placed across each arm and one across each leg. The interval between treatments was usually one week unless the urgency of symptoms suggested more frequent applications. The treatments have proved entirely harmless to young children, and if the symptoms are very urgent, a second dose may be given within a day or two after the first. In order to get results it is essen-

Figure 5

Figure 5a

Fig. 5.—M. E. before treatment, 3/12/17.
Fig. 5a.—M. E. after three treatments, 3/29/17.

tial that the treatments be comparatively heavy and that they be repeated at sufficiently short intervals. The failure to administer full doses and to repeat them promptly has in very urgent cases led to fatalities under Roentgen-ray treatment. Such a distressing occurrence is, fortunately, uncommon, but when it does happen it casts a doubt on the diagnosis or on the efficiency of the Roentgen-ray therapy. To guard against sudden deaths before the full destructive effect of the Roentgen ray on the thymus gland has been elicited, all patients with urgent symptoms should be kept under close observation and the Roentgen-ray treatments should be pushed boldly.

In the average case, improvement of symptoms has been noted within twenty-four to forty-eight hours after the treatment. It is possible, however, as shown by animal experimentation, to elicit changes

in the thymus gland within eight hours after the exposure. Therefore, the most urgent cases can be saved by this treatment.

The pictures here presented are taken from our patients at the Cincinnati General Hospital.

The thymus plates are shown in pairs for each case. First before treatment; second after treatment, with dates.

4 West Seventh Street.

THE VALUE OF THE VON PIRQUET TEST AS CONTROLLED BY NECROPSY FINDINGS *

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The object of this paper is to report the results of a study of the von Pirquet cutaneous test for tuberculosis on a series of children who have died and on whom careful necropsies have been performed. It is felt that in this way alone a conclusive judgment as to the value of the von Pirquet reaction in making a positive diagnosis of the presence or absence of tuberculosis can be acquired, for postmortem examination offers the only absolute verification of the diagnosis of tuberculosis.

Many investigations of this reaction have been made in this country on children from infancy through school age, in which the results of the test, whether positive or negative, have been confirmed by painstaking physical examination, or by means of the Roentgen ray — very exceptionally by the determination of tubercle bacilli. The discovery of tubercle bacilli, of course, must be accepted as indubitable evidence of the presence of tuberculous infection, but the examination of the chest by the most refined methods at our disposal assisted by Roentgen rays is still a gross and unsatisfactory method of establishing the absence or presence of tuberculosis in doubtful cases, and therefore cannot be used to verify with absolute certainty the value of the von Pirquet reaction. Confirmatory evidence of the reliability of this test has been furnished by a number of writers who have shown that the percentage of positive reactions in children increases with their age; that the danger from spreading and fatal tuberculosis is in inverse ratio to the age of the patient, and that tuberculous infection under two years is rarely recovered from.

Thus Rogers,[1] who followed fifty of the sixty-nine children with positive von Pirquet reactions after their discharge from the Massachusetts General Hospital, found that of the seventeen under 2 years of age, 65 per cent. died, whereas of the thirty-three over 2 years, but 21 per cent. succumbed in from one to four years.

The comparative infrequency of tuberculosis among young infants was shown by Voronin,[2] who examined 140 infants between 2 days

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1. Rogers, O. F.: A Study of Children with Positive Skin Tuberculin Reactions, Boston Med. and Surg. Jour., 1915, **172,** 161.

2. Voronin, M. S.: Tuberculin Skin Reactions, Russk. Vrach., 1915, **14,** 12, 280.

and 4 months of age, and obtained only two positive von Pirquet reactions.

Brown[3] performed the test on 650 children, 164 of whom were under 6 months, and of these, twenty reacted positively and all but one died.

Veeder and Johnston[4] as the result of von Pirquet tests on a large number of schoolchildren in St. Louis, between 10 and 14 years, found that 44 per cent. reacted positively to the von Pirquet test, as compared to 90 per cent. found by Hamburger in a similar investigation among children in Vienna. Veeder's results have been confirmed in many American cities and would indicate that tuberculosis, though all too prevalent, is less widespread in America than in most of the cities of Europe. This is probably due to the more favorable hygienic surroundings in this country, as Keifetz[5] has found that the positive von Pirquet reaction was obtained twice as frequently among children living among unfavorable surroundings as among those living in an environment described as favorable.

Von Pirquet's[6] report on the value of the cutaneous test for tuberculosis in children, is based on the examination of about 2,000 children. Of these, 200 died and came to necropsy. Of the fatal cases, 109 had no tuberculous lesions, while in eighty-nine, foci of tuberculosis were found, and two had doubtful lesions. The 109 children found at necropsy to be free from tuberculosis had negative skin reactions. Of the eighty-nine cases shown to have tuberculous lesions at necropsy, sixty had positive von Pirquet tests and twenty-nine had negative reactions. In the negative cases the reaction was made during measles, or on patients extremely ill with spreading or advanced lesions of tuberculosis.

The present study is based on investigation of the fatal cases that have come to necropsy from the Harriet Lane Home, of the Johns Hopkins Hospital, service of Dr. Howland, to whom I am indebted for the use of his material, from November, 1912, to April, 1917. In this time there were approximately 2,940 cases admitted to the wards, with 750 deaths. Of this number, careful necropsies were performed on 324 infants and children, from birth to 12 years of age.

These necropsy cases have been analyzed with reference to the von Pirquet reaction. Sixty-eight cases were found to have tuberculous lesions on postmortem examination, that is, about 20 per cent. of

3. Brown, A.: Am. Jour. Obst., 1913, **68**, 377.

4. Veeder, B. S., and Johnston, M. R.: The Frequency of Infection with the Tubercle Bacilli in Childhood, Am. Jour. Dis. Child., 1915, **9**, 478.

5. Keifetz, M. N.: Cutaneous Tuberculin Test in School Children, Jour. Am. Med. Assn., 1915, **65**, 1412.

6. Von Pirquet, C.: Summarized in Cleveland Med. Jour., 1908, **7**, 585.

the fatal cases examined after death. Two hundred and fifty-six, or 80 per cent., were found at postmortem examination to be free from tuberculosis.

This incidence of tuberculosis in infancy and childhood agrees with the results of Veeder's investigations and is much smaller than is reported in European centers. As has been repeatedly found, the number of tuberculous cases increased rapidly with the age of the patient.

The tuberculous and the nontuberculous cases have been tabulated according to age and color and with reference to the von Pirquet reaction.

TABLE 1.—Tuberculous Cases at Necropsy

	White			Black			Totals		
	+	—	Not made	+	—	Not made	White	Black	White and Black
Under 6 mo.	2			2	2	1	2	5	7
7 to 12 mo.	5	1		4	1	2	6	7	13
13 to 24 mo.	4	1		4	3		5	7	12
Over 2 yr.	7	4		17	4	4	11	25	36
Total	18	6	0	27	10	7	24	44	68

This test was made, where performed at all, as a routine measure by the ward intern. Koch's old tuberculin, undiluted, was used and the scarification done by the borer devised by von Pirquet. Readings were made in twenty-four and forty-eight hours. Of the 256 cases having no tuberculous lesions at necropsy, the test was made in 172 instances. It was never positive, but negative without exception.

On the original inspection of this series, there were four cases thought to be positive, but in carefully reviewing the histories it was found that in three instances, although the first test had been doubtful, a second confirmative test was negative, and in the fourth case, a patch of fibrous pleurisy, probably tuberculous, accounted for the postive skin reaction.

It should be emphasized that no doubtful cases should be called positive, but the test should be repeated; and only those called positive in which there is a marked contrast between the tuberculin treated areas and the control site. This result seems to furnish most reliable confirmatory evidence among American children that a properly performed von Pirquet reaction which is constantly negative precludes the possibility of tuberculous infection, except in extremely ill children.

Of the sixty-eight cases in which tuberculous lesions were found at necropsy, the von Pirquet reaction was made in sixty-one; of these, it resulted positively in forty-five cases and negative in sixteen. The negative cases were carefully analyzed. In twelve instances the patients were suffering from rapidly advancing widespread miliary tuberculosis, in two instances from tuberculous meningitis, in two from pulmonary tuberculosis of advanced stage with cavity formation, and in one instance from tuberculous peritonitis. In all instances the test had been made from a week to a few days before death, usually several weeks after the onset of illness.

TABLE 2.—Non-Tuberculous Cases at Necropsy

	White			Black			Totals		
	+	—	Not made	+	—	Not made	White	Black	White and Black
Under 6 mo.	0	41	25		34	27	66	61	127
7 to 12 mo.	0	21	10	0	17	6	31	23	54
13 to 24 mo.	0	19	3	0	15	3	22	18	40
Over 2 yr.	0	15	8	0	10	2	23	12	35
Total	0	96	46	0	76	38	142	114	256

It can be fairly concluded, therefore, from our figures, that as asserted by von Pirquet and repeatedly confirmed by other investigators, that a positive cutaneous test indicates the presence of a tuberculous lesion, but that a negative test in patients extremely ill, overwhelmed by the toxin of tuberculosis, especially in those suffering from miliary tuberculosis, may frequently fail to react positively. In

other words, a negative test, except in extremely ill patients in which the physical examination would probably determine the presence of tuberculosis, usually indicates the absence of tuberculous lesions, whereas a positive reaction in every instance shows the presence of tuberculosis. None of the patients in our series had measles.

The tabulation of the tuberculous cases shows that forty-four of the sixty-eight cases are colored, and twenty-four white; and of the seven fatal cases under 6 months, five are colored, and two white. These results would strengthen the view that tuberculosis is much more prevalent among the black than among the white races, in proportion to their population, and that the tuberculous infection occurs at an earlier period of life in the black.

It may be concluded from these results here reported that the cutaneous test with tuberculin, as described by von Pirquet, is a most reliable aid in the detection of tuberculosis in children; that a positive reaction indicates invariably a tuberculous focus in the body; and that a persistently negative reaction establishes the fact that there is no tuberculous lesion except in those extremely ill patients where the presence of tuberculosis can be readily established by physical examination.

INTRAVENOUS GLUCOSE INJECTIONS IN INFANCY *

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BOSTON

The principal difficulty attending intravenous injections and transfusion in young infants has always been a technical one due to the extremely small size of the veins. The suggestion of Helmholtz, that in hemorrhagic disease of the newborn transfusion could be more easily performed by using the longitudinal sinus, appeared to be of the greatest importance in this connection. The longitudinal sinus in the infant is a large vein easily accessible through the open fontanel. If the employment of this route in performing transfusion avoids the principal technical difficulty, it is available not only for transfusion in hemorrhagic disease of the newborn, but also for the giving of intravenous injections and medication. That certain forms of medication, as well as the giving of fluid for the purpose of stimulation or of supplying loss to the blood, are best given directly into the blood itself rather than by mouth or by the subcutaneous route, has long been recognized. This is particularly true, when it is desired to give normal salt solution or circulatory stimulants in certain cases in infants in which the condition is such that absorption from the skin takes place with great difficulty. Such a condition is seen in many cases of extreme atrophy and inanition.

At the Infants' Hospital we have adopted the use of the longitudinal sinus for obtaining blood for the Wassermann reaction and for giving intravenous injections. The technic has proved to be extremely simple and apparently entirely free from danger, except perhaps when salvarsan is used. We have used the longitudinal sinus for the giving of normal salt solution, of sodium bicarbonate in acidosis, of antitoxin in diphtheria, of circulatory stimulant drugs and of solutions of glucose. It is the glucose injections which are to be considered in this paper.

The cases in which the intravenous injection of glucose was used were all of approximately the same type. They were cases of a condition well known to all pediatrists, showing extreme atrophy and inanition produced by various forms of gastro-intestinal disease. Such cases are commonly admitted to the hospital in a moribund condition, especially in the summer and autumn months. Other cases are in less immediately serious condition when first admitted, but go down hill rapidly in spite of all our available therapeutic resources. In the treat-

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ment of these cases, in addition to the regular dietetic treatment of the underlying gastro-intestinal disability, we have such measures as the checking of excessive watery diarrhea with loss of salts by means of opium, the counteracting of a relative acidosis by the giving of sodium bicarbonate, and the giving of fluid by rectum or subcutaneously to supply loss and as a circulatory stimulant. All the cases reported in the present series were of infants who were either admitted to the hospital in an actually moribund condition, or, who after admission become steadily worse under all the ordinary methods of treatment.

The theoretical basis for the use of intravenous glucose injections in such cases is that apparently the vicious circle produced by gastro-intestinal disorder has become so extreme that the digestion and absorption of sufficient food to furnish the energy requirement of the body is impossible. Necropsies in such cases seldom reveal lesions of a character sufficiently pronounced to be considered the cause of death. We can only assume that death is produced either by lack of fuel, or by the accumulation of the toxic products of a metabolism disordered by the lack of fuel. Glucose is the only food substance which exists outside the body in the same form in which it circulates in the blood and is utilized by the tissues. All other food substances must go through the complicated processes of digestion and alimentary absorption before they can be used. Consequently, it seemed that the injections of glucose directly into the blood in these cases might, through a temporary supply of even a small quantity of fuel, break the vicious circle for a length of time sufficient to permit improvement of the condition to take place.

TECHNIC

The technic which has been used is very simple. A syringe sufficiently large to hold the entire quantity of fluid to be given is connected with the needle by means of flexible rubber tubing. There is a glass window in the tubing just above the needle. The needle is of a small size, such as is used for lumbar puncture in infants, slightly larger than an antitoxin needle. The entire apparatus is sterilized, and the syringe is filled with a sterile 5 per cent. glucose solution. After expulsion of any air which may be in the tube, the needle is entered at the posterior angle of the fontanel. Three persons are required to give the injection: one to steady the infant's head, one to manipulate the needle, and one to manage the syringe. The entrance of the needle into the sinus is accompanied by a sudden lessening of resistance. The piston of the syringe is then slightly and slowly withdrawn until blood appears at the glass window. As soon as the appearance of blood shows that the needle is actually in the sinus, the movement is reversed and the glucose is injected very slowly, the assistant holding the needle firmly in place. We have adopted the use of a syringe rather than the use of the gravity method because with the syringe and glass window one can make sure that the injection is actually going into the sinus. We have found no objection to the use of the syringe if the injection is given very slowly. A sign of too rapid injection of the fluid is distention of the superficial veins of the scalp. No accidents or unfavorable effects which could in any way be attributed to the intravenous injections have been observed with glucose solutions.

In determining the quantity of glucose to be injected, I rather arbitrarily adopted a 5 per cent. solution. I am inclined to think, however, that I shall try somewhat stronger solutions in the future. The quantity of the solution to be injected depends on the quantity of fluid which it is safe to inject into the infant's circulation. This, of course, is not definitely known, and I was obliged to adopt an arbitrary rule. We began with a quantity of fluid approximately equal to one fourth of the estimated blood volume of the infant. As this quantity of fluid appeared to produce no bad results of any kind, it was adopted as the standard for intravenous injections. The blood volume is estimated at approximately one fifteenth of the body weight, and therefore in choosing the quantity of glucose solution for intravenous administration to a baby, one sixtieth of the body weight is taken. The quantity of glucose given, therefore, varies with the body weight of the infant. With 5 per cent. solutions, it lies between 1 gm. as a minimum, which would be contained in 22 c.c. of fluid, and would be suitable for a baby weighing 1,320 gm., and 12 gm. of glucose, which would be contained in 240 c.c. of fluid, and would be suitable for a baby weighing 14,400 gm.

RESULTS

In eighteen cases the records are sufficiently complete to make them available for the purposes of this report. I do not wish to imply, however, that these cases are presented in statistical form as proof of benefit from the injections. Clinical evidence of improvement with any therapeutic procedure of this kind is very uncertain and can never be accepted as proof. Nevertheless, in some of the cases the improvement which followed the injections was so immediate and so striking that it seems to me there is a possibility at least that the injections produced a good effect. It must be remembered that all the cases were either actually moribund or were of a type in which all other measures had failed, and in which a fatal ending seemed imminent. Of the eighteen cases in which this treatment was used, thirteen died and five recovered. After the injections, seven cases showed no improvement, five cases showed a slight temporary improvement, and six cases showed a striking improvement immediately following the injections. There is no evidence that the improvement, even if it was due to the intravenous injection, was caused by the glucose. The giving of fluid into the circulation in cases of this character is a therapeutic procedure of known value, and it is quite possible that the apparent improvement was due to the fluid given and not to the glucose.

I have not on record a sufficient number of control cases in which normal saline solution was given intravenously instead of glucose to present any evidence on this point. Even if I had such a series of control cases, the evidence would not be of much value in pointing to the glucose as the cause of improvement. There is, however, sufficient possibility of the improvement being due to this therapeutic procedure to warrant its further trial.

There is certainly a possibility of the glucose being of value if it is actually utilized for purposes of energy production. Evidence on this

TABLE.—Results of Urinary Examination

Case No.	Dates of Injection	Quantity of Glucose Given (Gm.)	Quantity of Glucose Eliminated (Gm.)
1	October 15	1.5	0.074
	October 16	3	0.220 +
	Total	4.5	0.294 +
2	October 12	0.75	0
3	October 2	6	0
4	October 25	3	0.068
	October 27	3	0.116 +
	Total	6	0.184 +
5	October 31	4.5	?
6	September 23	3	0
7	September 23	3	0.112 +
8	September 16	3	0
9	November 4	2.25	Slight trace
10	September 14	1.5	0
	September 16	2.25	Slight trace
	October 2	1.875	0
	October 17	2.25	Slight trace
11	October 29	3	0.086
12	August 28	3	0
13	September 27	4.5	0.047 +
14	September 14	3	0.08
	September 16	3	Slight trace
	Total	6	0.08
15	September 11	3	0
	September 12	3	0
	September 15	3	0
	September 16	3	0
	September 17	3	0
	September 18	3	0
	Total	18	0
16	August 28	3	Slight trace
17	July 12	3	?
18	July 1	1.5	0

point can be obtained from the examination of the urine because glucose in the blood not utilized is excreted through this route. Efforts were made in all the cases of the series to determine what proportion of the glucose given by intravenous injection was not utilized and was excreted by the kidneys. For this purpose, all the urine passed after the injection was collected for twenty-four hours, or until it was sugar-free. A quantitative estimation was made of the sugar excreted. For the quantitative tests, Benedict's solution was used. The table shows the results of the urinary examination in these cases. A question mark in the column showing the quantity of glucose eliminated means that the patient died before any urinary examination could be made. The plus sign after the figure in the same column shows that the patient died before the urine became sugar-free and that, therefore, the figure does not represent the total quantity eliminated. The term "slight trace" in this column means that the urine gave a qualitative reaction to sugar with the most delicate reagent (Folin's), but that the amount of sugar was too small to measure by the quantitative test.

It will be seen from the table that in the great majority of instances either no sugar was eliminated in the urine after the intravenous injections, or else there was only a slight trace. Only in six instances was a measurable quantity of glucose eliminated, the maximum quantity eliminated in any instance being 220 mg., or only 0.66 per cent. of the quantity of glucose injected into the blood. These results appear to prove that whether or not the glucose produced a favorable effect, it was at least utilized by the child's metabolism. With such utilization there is certainly a possibility of a favorable effect even from the small quantities of glucose which were given.

The table shows that only one injection was given in the majority of the cases in the series. This is because so many of the patients showed no notable improvement or died soon after the giving of the injections. In five cases more than one injection was given, these corresponding to three of the cases in which the patients eventually recovered and to two of the cases in which the patients showed a marked improvement but died at a subsequent period. In Case No. 15, six daily injections of 3 gm. of glucose each were given. In this case, it seemed to us that the patient was practically kept alive by the glucose injections, and that recovery was due to this method of treatment. This patient eliminated no sugar in the urine at any time.

The diseased condition which these cases represent is very serious and fatal, and it seems to me that in its treatment we have need of every possible therapeutic resource. It is my hope that further trial will either add to the slight evidence which I have presented as pointing to the possible value of intravenous glucose injections, or will conclusively disprove the value of this therapeutic procedure.

POSTOPERATIVE ACID INTOXICATION *

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AND

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For the past twenty years or more there has been an increasing literature reporting serious and fatal illness in children following surgical operation, the illness apparently having no direct relation to the immediate effects of the anesthetic or the operation. This condition, characterized by vomiting, thirst, flushed face, somnolence and restlessness, and, in the more severe cases, by delirium, coma and death, has been known by a variety of names, but the general idea pervading the literature and expressed in the various names has been that it is an acid intoxication closely associated with or caused by the acetone bodies. A few authors have taken exception to this view on the ground that the accumulation of acids in the body in the condition described has never been proved, though no other evidence is offered in their support. Though there is a large and ever-increasing number of articles dealing with the subject, there remains an absence of rather essential data for the better understanding of this phenomenon. It was with the hope of answering some of the unsettled questions that the work of this paper was undertaken. It might be added that at the beginning of the observations a strong prejudice toward the acetone body causation of the condition was entertained.

Material Studied.— The points to be emphasized here are based largely on the study of twenty-two operative cases. These were taken consecutively and not selected in any way, though it so happened that among them there were no cases showing the symptoms above described, and the group also happens to represent very little emergency surgery. All patients were anesthetized with ether by the same professional anesthetist. In these twenty-two cases the urine was examined in twenty-four-hour periods before and after operation, and the blood before and at frequent intervals after operation, the observations being continued for at least forty-eight hours after operation, and when indicated, for seventy-two hours. In the urine were determined the acetone bodies and the ammonia coefficient, and in the blood the acetone bodies and the plasma carbonate.

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* From the Department of Pediatrics, Washington University Medical School, and the St. Louis Children's Hospital.

The acetone bodies of the urine were determined by the iodimetric method of Messinger and the oxidation method of Shaffer.[1] The nitrogen of the urine was determined by the micro-methods of Folin.[2] The acetone bodies of the blood were determined by the method of Marriott[3] and the plasma carbonate by the method of Van Slyke.[4]

Acetone Bodies in the Blood.—Accepting 10 mg. total acetone bodies (estimated as acetone) per 100 c.c. of blood as the upper normal limit, it was found that of the twenty-two cases mentioned, fourteen, at one or more observations, gave values above the normal, while eight at all times gave values within the normal limit. The maximum value found was 53 mg., which was reached twenty-four hours after operation. Twenty of the twenty-two cases reached their maximum acetone body content of the blood in the first twenty-four hours. In three of these the maximum was reached one, six and eleven hours after operation, and in two of the three the high value was maintained through the first twenty-four hours. Two cases gave quite normal values during the first twenty-four hours, but by the end of the second twenty-four hours had reached a maximum of 33 and 35 mg. The maximum content in most instances was found near the end of the first twenty-four hours, and the average content at this time was 15.7 mg.

In another group of twenty cases having ether as an anesthetic, there was found twenty-four hours after operation an average content in the blood of 13.4 mg., and in a group of thirty-seven cases having nitrous oxid as an anesthetic there was found twenty-four hours after operation an average of 16.7 mg. The average of seventy-nine cases of the three groups was 15.6 mg., with a maximum value of 61 mg.

Plasma Carbonate.—Accepting 50 vol. per cent. as the lowest normal value, it was found that of the twenty-two cases described, nine cases at all times gave values within the normal limits. Values below 50, at one or more observations, were obtained in thirteen cases, and below 40 in seven cases, the lowest value obtained being 32.4 vol. per cent. Of the thirteen cases giving values below 50 vol. per cent., ten had their minimum value in the first twenty-four hours, seven of these having their minimum value near the end of this period, while three cases had the minimum value at the first observation, one, one and six hours after operation. The remaining three cases had their lowest value at twenty-eight, thirty-four and forty-eight hours after operation.

1. Shaffer, P. A.: Jour. Biol. Chem., 1913, **16,** 265.
2. Folin and Farmer: Total Nitrogen, Jour. Biol. Chem., 1912, **11,** 493; Folin and Macallum: Ammonia Nitrogen, Jour. Biol. Chem., 1912, **11,** 523.
3. Marriott, W. McK.: Jour. Biol. Chem., 1914, **18,** 507.
4. Van Slyke, D. R.: Unpublished.

Acetone Bodies in the Urine.—In the twenty-two cases described the acetone bodies of the pre-operative urine specimen were normal in amount in all except one case, in which there was but a slight increase. The maximum excretion of total acetone bodies (estimated as acetone) in the first twenty-four hours after operation was 2.36 gm., and in the second twenty-four hours was 5.38 gm., these values being obtained in different cases. The excretion in several patients after operation did not differ from the normal, and in one-third of the cases the amount in the second twenty-four hours was less than that in the first. There was an average excretion of 0.46 gm. in the first twenty-four hours and of 0.9 gm. in the second. The higher acetone values in the second twenty-four hours are the natural result of the higher blood acetone values obtained in the latter part of the first twenty-four hours. Another group of twenty-seven operative cases having ether anesthesia, gave an average acetone body excretion for comparable periods after operation practically identical with that of a group of thirty-six cases having nitrous oxid.

Ammonia Coefficient in the Urine.—After having determined the plasma carbonate, the ammonia coefficient of the urine is relatively of but little value, since the latter when increased is merely indicative of an increase of acids or a need of alkali in the body, while the former may be taken as conclusive evidence of an alkali need and as good presumptive evidence of an acid increase. The ammonia coefficient gives some idea as to the amount of base spared to the body by this means of body defense. In the twenty-two cases of this study there was found in the preoperative specimen an average ammonia coefficient of 7.4 with a maximum of 12. In the first twenty-four hours after operation there was found an average coefficient of 8.6, with a maximum of 16.9, and in the second twenty-four hours was found an average of 9.5 with a maximum of 19.3. The higher coefficient in the second twenty-four hours after operation corresponds to the maximum plasma carbonate reduction in the latter part of the first twenty-four hours.

Comparison of the Increase of Acetone Bodies with the Decrease of Plasma Carbonate.—Roughly, and in a general way, we find in these cases a certain parallelism between the decreased carbonate and the increased acetone bodies of the blood. We find in most instances the largest amount of blood acetone bodies toward the end of the first twenty-four hours, and likewise, in most instances, the lowest carbonate values at about the same time. A brief glance at the following table, however, will show the decided absence of any close association as determined in these cases.

These blood findings are corroborated by the urine examination. In Case 5 is found a total excretion of acetone bodies for forty-eight

hours after operation of 0.144 gm., and the low carbonate is corroborated by finding an ammonia coefficient in the second twenty-four hours after operation of 19.3.

In Cases 5, 6 and 9 there is observed a much reduced plasma carbonate with a practically normal acetone body content of the blood. In the other cases, though the acetone bodies are increased, they are not increased sufficiently to reduce the reserve alkali to the extent indicated, even if increased ammonia production is left out of consideration. In all of these cases the excess of ammonia in the urine is more than sufficient, and in several cases, several times the amount that would be required to neutralize the acetone bodies excreted at the same time.

Table Showing Findings in Authors' Cases

Case	Blood Carbonate Vol. Per Cent.	Total Acetone Bodies 100 gm. Blood	Interval in Hours
1	39.2	31.0	
2	52.2	26.0	
	45.6	9.8	24
3	44.9	28.4	
	39.2	22.2	6
	48.3	23.6	27
5	45.4	11.8	
	32.4	12.0	5
	53.2	4.0	20
6	37.6	2.7	
	40.0	3.0	7
	39.8	7.0	8
	52.9	8.2	6
9	45.7	2.3	
	43.8	2.7	4
	50.0	3.5	5
15	33.4	53.0	
	46.3	51.0	9
20	44.0	39.0	
	39.4	37.0	11

It is evident that in these postoperative cases, which were asymptomatic as far as acid intoxication is concerned, there occurs an acid factor other than the acetone bodies, and that this factor is quantitatively important. That the same acid factor may occur in cases showing hyperpnea and other symptoms ascribed to acid intoxication, is shown by observations on a patient operated on for ruptured liver,

which case did not fall into the routine study that was made on the twenty-two cases described. This patient showed in the blood 44.5 mg. total acetone bodies per 100 c.c., and at the same time 24 vol. per cent. plasma carbonate. Such an amount of acetone bodies could not possibly have reduced a normal plasma carbonate to this dangerous level.

As an illustration of an instance in which the acetone bodies alone fully account for the reduction of plasma carbonate, may be cited a case of cyclic vomiting in which was found an acetone body content in the blood of 107 mg. per 100 c.c., associated with a carbonate content of 36.2 vol. per cent. A larger series of postoperative cases might reveal instances in which a much reduced blood carbonate could be largely or wholly accounted for by the amounts of acetone bodies found, but the point we wish to make is that, contrary to much current opinion and our own previous prejudice, there has been shown by this study to be some very important factor in the production of low carbonate content of the blood other than the increased production of acetone bodies. That the margin of safety for the patient would be greater were the acetone bodies not increased there can be no doubt, and the measures now in common use directed against the acetone increase, if shown to be effective, still have their field of usefulness.

The Rôle of Starvation.—That the acetone bodies are increased in starvation is a matter of common knowledge, and that there are other factors than starvation in the acetone production of operative cases seems certain from our observations. Though there is some factor that we may inadequately describe as personal idiosyncrasy in the reaction to starvation, a serious acidosis caused by simple starvation of the duration commonly incident to surgical operation does not seem probable. In seven apparently normal children, subjected to simple fast for forty-eight hours, there was found in the blood at the end of the first twenty-four hours an average of 39.3 mg. total acetone bodies, with a maximum of 72 mg., and at the end of the second twenty-four hours was found an average of 68 mg., with a maximum of 106 mg. None of the children showed any sign of illness. That starvation does not necessarily produce a marked increase of the acetone bodies was shown by a patient who five days after the institution of a therapeutic fast showed 6.6 mg. acetone bodies per 100 c.c. of blood, with a plasma carbonate of 50.5 vol. per cent., and at the end of eight days of fast had 22.6 mg. acetone bodies with a plasma carbonate of 56 vol. per cent. In a study of acetone body formation as a result of fast now being made in this clinic by Veeder and Johnston, several cases have been encountered in which the acetone bodies were but slightly increased, and in all the cases so far studied by them the blood carbonate reduction has not been greater than could be adequately accounted for by

the amount of acetone bodies found, and it may be concluded that starvation itself does not enter into the unknown acid factor described for the operative cases.

SUMMARY

The acetone bodies of the blood were somewhat increased after operation in about two-thirds of the children studied, the maximum amount being found in most instances about twenty-four hours after operation. The plasma carbonate was reduced in about two thirds of the cases, the greatest reduction occurring in most instances about twenty-four hours after operation. When more closely compared there was found to be no close relation between the increase of acetone bodies and the reduction of plasma carbonate. In most instances, especially in those cases in which the plasma carbonate was much reduced, the acetone bodies were entirely inadequate to account for the degree of reduction of plasma carbonate. The undetermined acid factor was apparently of much greater importance than the acetone bodies in the reduction of reserve alkali. The starvation incident to operation seems to play no part in the production of this undetermined factor.

INTUSSUSCEPTION OF THE BOWEL IN AN INFANT

FOLLOWED BY OBSTRUCTION OF THE BOWELS WITH A SECOND INTUSSUSCEPTION WITHIN THREE WEEKS AFTER THE FIRST OPERATION *

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History.—Ann J., born Feb. 18, 1915, was taken ill during the evening of June 14, 1915, with some abdominal distress. The family physician, Dr. S. Peskind, saw the child the following day and, suspecting intussusception, advised the child's immediate removal to the hospital. The child arrived at the East Fifty-Fifth Street Hospital June 15 and was taken to the operating room at 5:30 p. m.

First Operation.—The lower end of the ilium, appendix, cecum, and part of the ascending colon were found telescoped into the transverse colon. When liberated the incarcerated bowel appeared very dark—gangrenous in spots. The age of the child and a pulse scarcely perceptible while under anesthesia precluded any attempts at resection of the devitalized viscus. The appendix, almost black in appearance, was quickly tied off and removed. The wound was closed and the child left the operating room with a very feeble heart action. The operation itself required less than fifteen minutes. At 6:15 p. m. the baby, then in its bed, had a temperature of about 100 F., pulse over 180, respirations between 56 and 60. The child, as soon as she recovered from the anesthetic, was given a few drops of Vichy water every ten or fifteen minutes and was put to the mother's breast for a few minutes at 10 in the evening. The child vomited a few times after the operation. A saline injection was given at 11 in the evening, which was expelled with flatus and was tinged with blood. The following day the temperature went up to 103.2 F., pulse 180 and over. Within forty-eight hours the temperature and pulse reached the normal. The recovery seemed complete within nine days and the little patient was sent home June 24, apparently free from signs of any gastro-intestinal disturbance.

Second Operation.—At 10:15 a. m., July 8, just three weeks after the first operation, the child was brought back to the East Fifty-Fifth Street Hospital with symptoms of acute obstruction of the bowels. Some resistance was felt in the cecal region, also in the middle of the transverse colon. The child looked hopelessly ill. The abdomen was opened and several inches of the ascending colon were found telescoped in the transverse part of the colon. This second intussusception was easily released and the bowel had a normal appearance. At the site of the first intussusception, however, were found the greatest foci of pathologic activity. The cecum and part of the ilium were both matted and bound together by unyielding adhesions. The lumen of the bowel felt as if it were obliterated. The only chance for the restoration of the continuity of the lumen of the bowel was to resort to ileocecostomy, and this was done. The child, not quite 5 months old, bore the operation seemingly without any additional shock. It required just twenty-six minutes to disengage the intussusception, to make the anastomosis, and to close the abdominal wound. Scarcely any gastro-intestinal difficulties followed the second operation, but

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a double pneumonia developed on the third day and the baby had to fight for its life for nearly two weeks. The temperature often exceeded 105 F. and the pulse rate over 180 per minute. The child remained in the hospital about a month after the second operation and was sent home Aug. 10, 1915. It is now a year and nine months since the child was operated on and at no time since has she evinced any sign of intestinal or pulmonary disturbances.

The interesting points to be drawn from this case are that it is almost impossible to measure with certainty a baby's power of resistance, and at the same time it emphasizes to me the seriousness of the surgeon's position in such cases, when he dares attempt the possibility of saving a human life in spite of apparent hopelessness.

2414 East Fifty-Fifth Street.

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EPIDEMIOLOGIC DATA IN THE POLIOMYELITIS EPIDEMIC IN NEW YORK STATE *

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While it cannot be said that any really new facts have been established regarding poliomyelitis as the result of last summer's great epidemic, certain more or less widely accepted opinions concerning the periods of infectivity, the age and sex incidence and the behavior of the disease under urban and rural conditions of living have been placed on a more solid scientific footing. I shall purposely omit statistical results of serum treatment, as I do not believe it possible at present to pronounce a definite opinion as to its value.

ORIGIN, SPREAD AND MAGNITUDE OF THE EPIDEMIC

The number of cases of poliomyelitis reported in New York State during the first five months of 1916 (forty-one) was quite low; in fact, below normal, affording no intimation of the sudden flare-up that was to follow. The general invasion of the state seems to have come from the Borough of Brooklyn, where the epidemic started in the second week in June, and within a month had caused a thousand cases a week in the greater city alone, during the week ending July 16.

Chart 1, tracing the course of the epidemic week by week, shows that in the state outside New York City the disease did not assume epidemic proportions until several weeks later, and ran its course much more gradually. It spread along the routes of travel out of New York City, particularly to the suburban towns and villages on Long Island, across the river into New Jersey and northward into Westchester. It then invaded the counties bordering on the Hudson River, and along the railroad lines leading north and northwest out of the greater city. The disease often "jumped" communities in the most astounding way. Many of the local outbreaks in the Catskill counties and up the Hudson were clearly traceable to imported cases brought in from New York

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City. In the central and northern parts of the state the epidemic did not reach its height until well along in August, and did not subside until the latter part of October.

During the period from June to December, 1916, there occurred in New York State over 13,000 cases and 3,300 deaths. Of the total number, 8,991 cases, or more than two thirds, occurred in New York City, the rest of the state reporting 4,186 cases.

COMPARATIVE INCIDENCE AND FATALITY OF THE DISEASE UNDER URBAN AND RURAL CONDITIONS

Table 1, together with Chart 2, shows strikingly the difference in the prevalence and fatality of the epidemic in the different sections of the state.

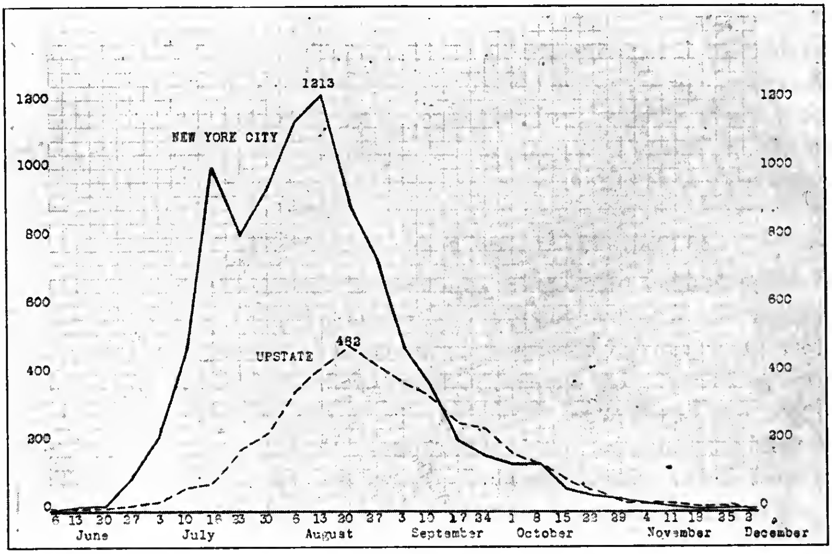

Chart 1.—Reported cases of poliomyelitis, week by week, during the epidemic of 1916 in New York City (dates of report) and upstate (dates of onset).

It will be noted that the districts affected in rural New York comprised but one half of its total population, while very few of the cities escaped the disease altogether. On the other hand, in those districts of rural New York that were affected, a much higher proportion of the population was attacked with poliomyelitis than in either New York City or the upstate cities. Thus, on the average, 2.4 persons per thousand population in the rural sections affected were attacked by the disease during the course of the epidemic, as compared with 1.6 in New York City, and 0.6 per thousand in the upstate cities as a whole.

TABLE 1.—Incidence and Fatality from Poliomyelitis During the Epidemics of 1916 and 1912

Area	Population of Areas Affected	Number of Cases	Case Rate per 10,000 Population	Number of Deaths	Fatality Rate per 100 Cases	Death Rate per 10,000 Population
June-December, 1916 New York City........	5,602,841	8,991	16.0	2,444	27.2	4.4
Upstate cities.......... (Total Pop., 2,279,047)	2,120,538	1,300	6.1	294	22.6	1.4
Rural New York....... (Total Pop., 2,417,814)	1,223,424	2,886	23.6	572	19.8	4.7
July-October, 1916 Newark, New Jersey...	366,721	1,390	37.9	372	26.8	10.1
1912 Buffalo, New York.....	423,711	297	7.0	39	13.1	0.9
New York state........ (Cases observed by Surgeon Frost)	....	1,108	....	183	16.5	

TABLE 2.—Movement of Cases, Deaths and Fatality Rates from Poliomyelitis During the Epidemic of 1916 in New York State, by Months

Month	State of New York			New York City			Rest of State		
	Cases	Deaths	Fatality Rate per 100 Cases	Cases	Deaths	Fatality Rate per 100 Cases	Cases	Deaths	Fatality Rate per 100 Cases
June.......	367	64	17.4	313	63	20.1	54	1	
July.......	4,011	895	22.3	3,443	779	22.6	568	116	20.4
August....	5,987	1,466	24.5	3,927	1,080	27.5	2,060	368	17.9
September.	1,992	628	31.5	985	364	37.0	1,007	264	26.2
October....	645	215	33.3	258	122	47.3	387	93	24.0
November.	135	40	29.6	47	25	53.2	88	15	17.0
December..	40	20	50.0	18	11	61.1	22	9	40.9
Total....	13.177	3,310	25.1	8,991	2,444	27.2	4,186	866	21.1

Table 2 shows the movement of cases, deaths and fatality rates by months, from June through December. Of the 13,177 cases reported in New York State during that period, 3,310 patients died, indicating a fatality rate of about 25 per cent., or one death out of every four cases, which is much higher than that observed in any considerable epidemic hitherto recorded. As between the different sections, it is notable that in the rural sections a much lower proportion of the cases proved fatal than in the cities. From Chart 2 (darkened portions) it

will be seen that 19.8 per cent. of the rural cases ended in death, the upstate cities following with 22.6 deaths per one hundred cases, and the New York City cases showing a decidedly higher proportion of fatalities than either of the other two areas — 27.2 per cent.

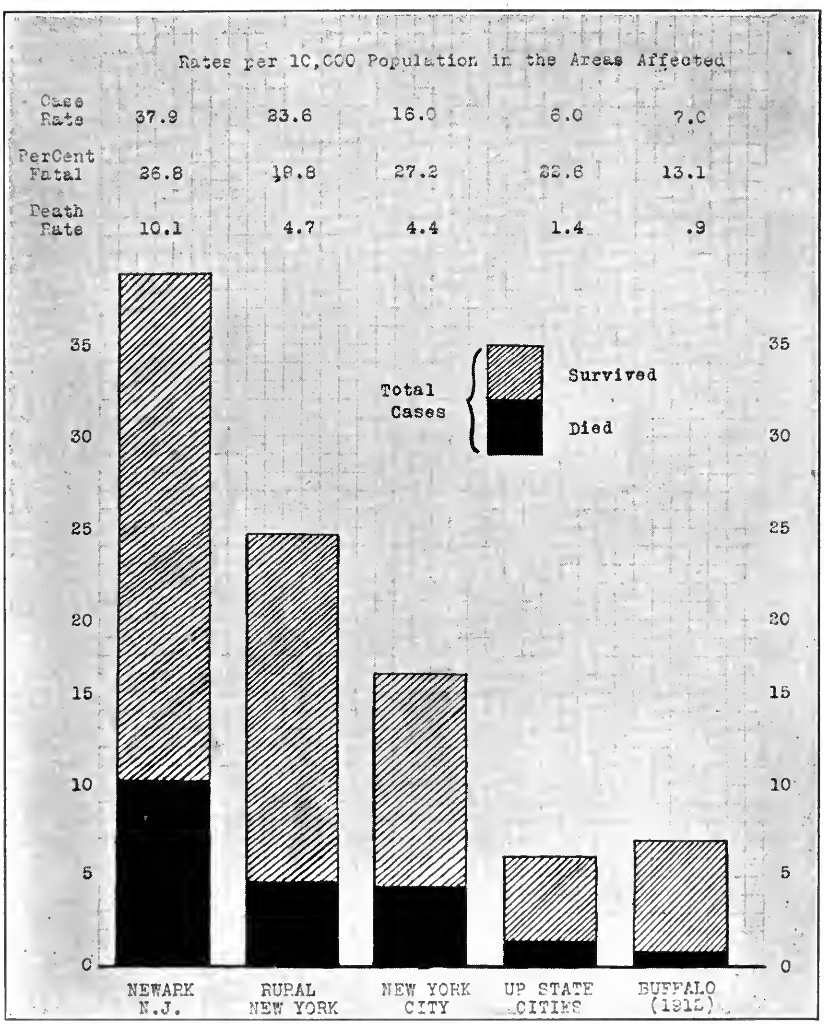

Chart 2.—Relative severity of poliomyelitis epidemic of 1916 in certain areas, judged by the comparative incidence and death rates recorded.

Whatever the explanation, apparently epidemic poliomyelitis, once it has entered a community, tends to be more widespread, but less virulent, under sparsely settled conditions of life than in the centers of population.

INFLUENCE OF SEX

The number of deaths among males was 50 per cent. higher than among females. Practically the same proportions — 60 and 40 per cent. — were observed in New York City and upstate, at the different ages, and from month to month. A study of the case figures shows that not only were boys more likely to be attacked than girls, but also that the disease is somewhat more fatal to males than to females. This is confirmed by the observed experience in the Newark epidemic.

DIFFERENCE IN AGE INCIDENCE IN CITY AND COUNTRY

One of the striking features of the epidemic was the fact that its rural incidence showed a noticeably different age distribution from the urban. An analysis of the first 7,500 cases in New York City shows that almost 80 per cent. were among children under 5 years of age; over 95 per cent. under 10, and over 98 per cent. under 16. Here, apparently, poliomyelitis was almost entirely a disease of children.

In the upstate cities, less than two-thirds of the patients were under 5 years, 86 per cent. under 10 and over 7 per cent. beyond the age of 15. In rural New York only 55 per cent. of the cases occurred among children under 5 years of age, half as many between the ages of 5 and 10, and 10 per cent. of all cases among persons older than 15 (Table 3).

TABLE 3.—Age Distribution of Cases and Deaths from Poliomyelitis During the Epidemic of 1916 in Different Sections of New York State

Age	New York City (June–Aug., 1916)		Upstate Cities (June–Dec., 1916)		Rural New York (June–Dec., 1916)	
	Number	Per Cent.	Number	Per Cent.	Number	Per Cent.
Total cases	7,496	100.0	1,300*	100.0	2,886*	100.0
Under 5 years	5,902	78.7	840	64.6	1,575	54.6
Under 10 years	7,157	95.5	1,114	65.7	2,365	82.0
Under 15 years (N. Y. C. under 16)	7,367	98.3	1,204	92.6	2,596	90.0
Over 15 years (N. Y. C. over 16)	129	1.7	96	7.4	290	10.0
	(Jan.-Dec., 1916)					
Total deaths	2,448	100.0	294	100.0	572†	100.0
Under 5 years	1,928	78.8	174	59.2	260	45.5
Under 10 years	2,315	94.6	242	82.3	406	71.1
Under 15 years	2,375	97.0	264	89.8	462	80.9
Over 15 years	73	3.0	30	10.2	109	19.1

* Ninety-seven cases of unspecified age in the upstate cities and 182 in rural New York were distributed in proportion as the known cases.
† Includes one death of unknown age.

Due to the higher fatality of poliomyelitis among adults, when the age distribution of the deaths is considered, the contrast between the different sections is even more pronounced. It will be seen from Chart 3 that while in New York City nearly four out of every five deaths were in children under 5 years of age, and 97 per cent. of all deaths occurred among persons under 15, in the rural sections only 45.5 per cent. were under 5 years, and 80.9 per cent. under 15, with fully 19.1 per cent., or one out of every five deaths, occurring among adults, persons beyond the age of 15.

In New York City the proportion of adults in each age period remained fairly constant from month to month during the course of the epidemic, while in the state outside New York City the age inci-

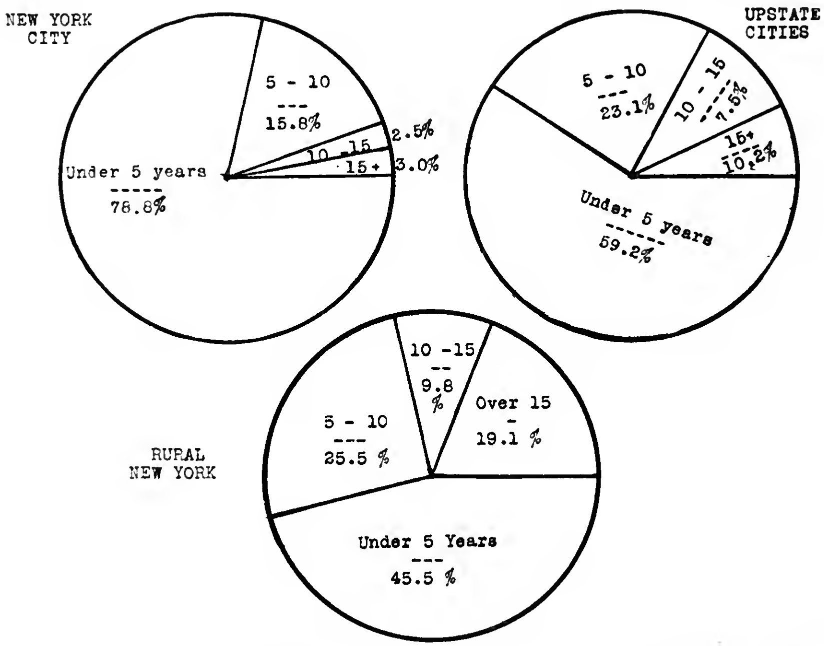

Chart 3.—Comparative age distribution of deaths from poliomyelitis during the epidemic of 1916 in New York City, upstate cities, and rural New York.

dence underwent considerable change with the progress of the epidemic. With the extension of the age limit upstate, it was observed that the proportion of deaths in the early ages decreased, and that at the later ages increased.

HAS THE RURAL POPULATION A LESSER DEGREE OF ACQUIRED IMMUNITY?

The experience of New York State with regard to the difference between urban and rural sections in age incidence of the disease is confirmed by the experience of other states during the epidemic of

1916. At the Cincinnati conference, Surgeon Frost of the U. S. Public Health Service, declared that "in rural epidemics, especially those in Iowa and Minnesota, a much larger proportion of the cases has been in the higher age groups than has been the case in epidemics occurring in large cities." Dr. Frost suggests an explanation for this difference when he says: "Certain other infectious diseases, notably measles, are largely limited to children, not because they are essentially children's diseases, but because the adult population has been more or less immunized." It seems not unlikely, therefore, that the limitation of poliomyelitis in urban epidemics almost entirely to children may be due to the fact that adults had developed a certain degree of immunity, through mild and perhaps unrecognized attacks in their early years; while the persons in more sparsely settled areas, who had been less exposed to the contagion of the disease in their childhood, had not acquired the degree of immunity which would render them able, as adults, to resist the infection when present in epidemic form.

RELATIVE FATALITY OF POLIOMYELITIS AT DIFFERENT AGES

A detailed analysis of the records of the 1916 epidemic brings out several interesting deductions as to the prognosis of poliomyelitis at different ages and under varying conditions. Chart 4 compares the proportion of cases proving fatal at each age period under urban and rural conditions. It will be seen at a glance that the disease was most fatal among infants under 1 year of age and to persons over 15. Thus, the chances of an infant surviving an attack of poliomyelitis in its first year of life were only half as good as that of a child a year or two older. After the third year the fatality rate rose with age, until among persons over 15, on the average one case out of three ended in death.

It will be noticed, too, that, up to the age of ten, the country child had a much better chance of surviving an attack than did the city child. With adults, however — that is, beyond 15 years of age — the advantage was on the side of the city bred.

THE FACTOR OF CONTACT

From an intensive study of individual outbreaks the State Department of Health has been able to obtain fairly conclusive evidence that contact is the immediate factor in the spread of an epidemic. Of 756 upstate cases that were tabulated and studied in detail, 91 cases, or 12 per cent. were definitely stated as associated with other cases in the same family, and 63 more were reported as having been in contact with other cases, making a total of 154, or 20.4 per cent. of all cases, which were known to have been associated or in contact with other or previous cases of poliomyelitis. In outbreaks of diseases which are

known with certainty to be transmitted by contact, seldom has so large a proportion of cases been definitely traced to contact.

An interesting example of a group of such definitely traced contact

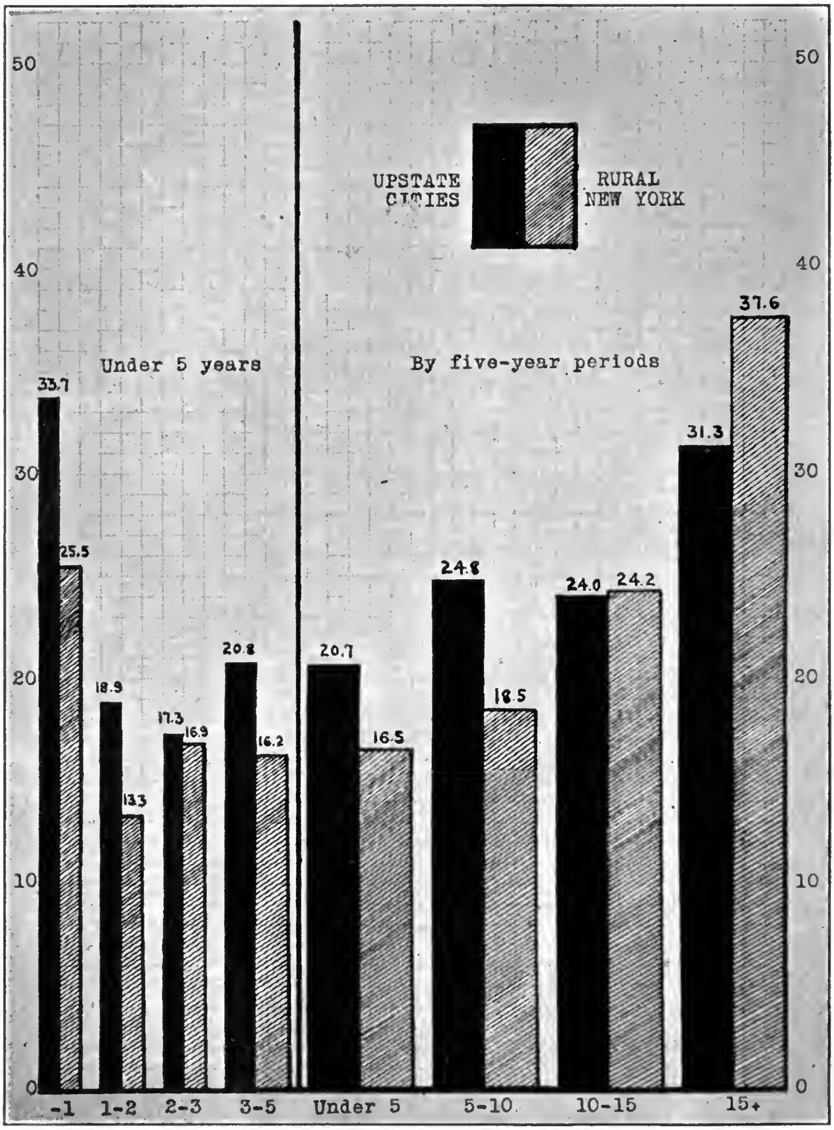

Chart 4.—Proportion of cases of poliomyelitis proving fatal at each age period during the epidemic of 1916 in upstate cities and rural New York.

cases, reported from a rural section of a northern county, is shown on the diagram (Chart 5). Note the various modes of contact by which

the disease was transmitted from C. C., the original patient of the group, to five others, of whom three died, and from them to three others closely associated with them. Note also the range of the ages — from 3 to 53 — with three of the eight known cases among persons beyond the age of 15. Of interest, too, is the period of incubation of the secondary cases. Judging from the difference between the time of exposure and date of onset, the incubation period of this group varied from eight to eleven days; half of them developing in eight days.

THE SAUGERTIES EPIDEMIC AS A TYPICAL OUTBREAK

The accompanying diagram (Chart 6), showing the incidence and association of poliomyelitis cases in the Saugerties epidemic of 1916, tells in graphic form the story of a fairly typical outbreak and how it was apparently controlled.

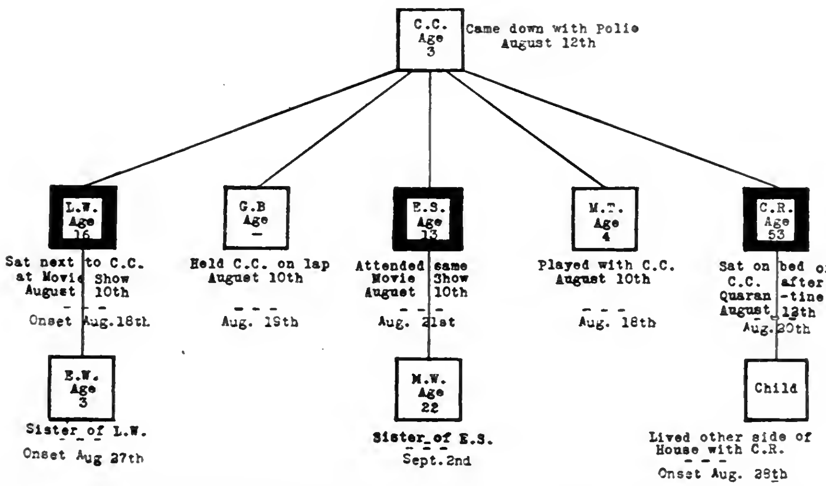

Chart 5.—Development of a contact group of poliomyelitis cases in Jefferson County during August, 1916.

Saugerties town and village form a consolidated health district, with an all-year population of 9,000 to 10,000, on the western bank of the Hudson River about 100 miles above New York City. The local epidemic seemed clearly an imported one, starting with a case coming from Brooklyn and reported to the health officer July 21. Within eight days five cases of the disease were reported in Saugerties, and then for a period of two months there developed an average of two cases a week. During the latter part of September there was a flare-up, eleven new cases developing between the 23d and 30th of the month, and fifteen cases more during the first two weeks in October.

According to the report of Dr. Charles W. Berry, sanitary supervisor, "a rigid quarantine was instituted as each case was reported,

but it did not seem very effectual in checking the disease. An investigation disclosed the fact that few of the cases were reported until actual paralysis had set in. All patients in the prodromal stage and during the period of acute symptoms before the onset of demonstrable paralysis were in full contact with other members of the household and such other persons as cared to go in and out of the sick room."

At this point, October 15, occurred the striking feature of this outbreak. A meeting of all local physicians was called that evening, and

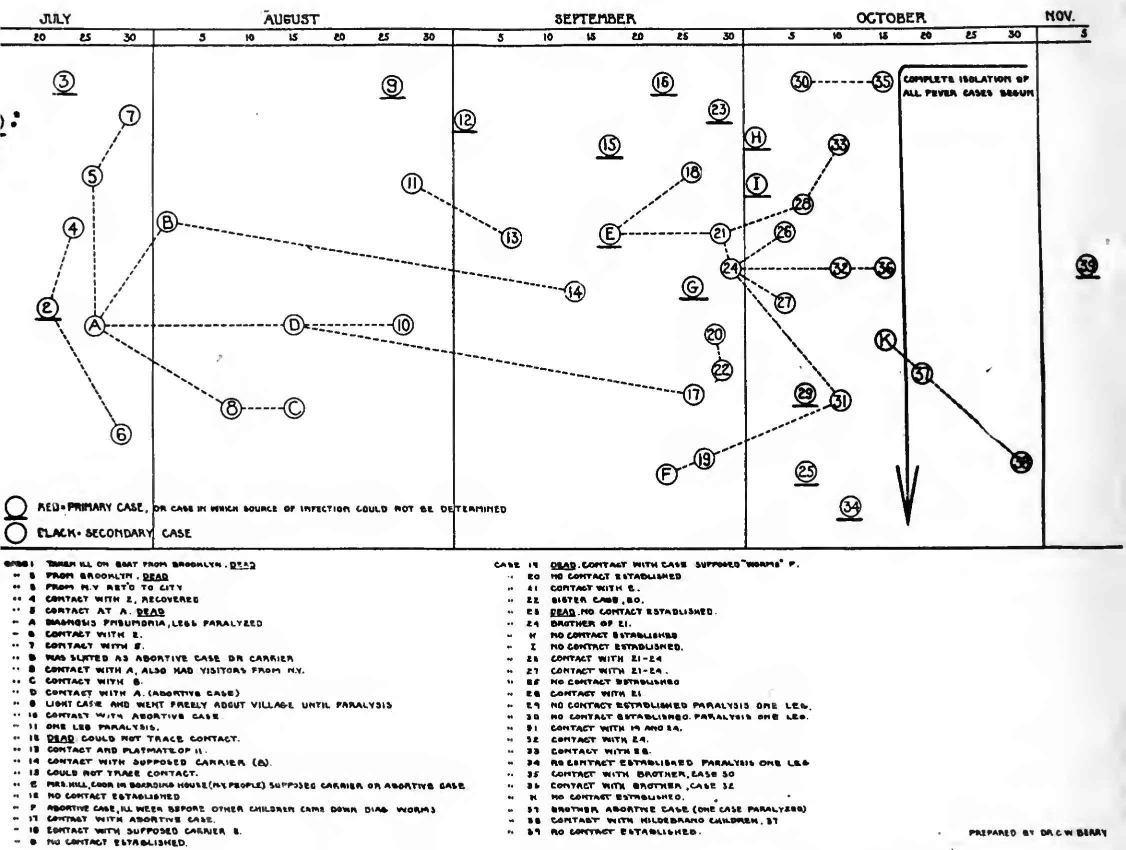

Chart 6.—Incidence and association of poliomyelitis cases in the Saugerties epidemic of 1916, showing the effect of complete early isolation of all fever cases after October 15.

a pledge obtained from each physician to isolate every case of fever that came under his care until a positive diagnosis of the cause could be made. This measure, coupled with the employment of a public health nurse for three weeks, who made daily inspection of all school children, followed up absentees, traced up contacts, and enforced strict

quarantine, appears to have been the means of securing effectual control of the epidemic.

Within the five days previous to the holding of the meeting on the evening of October 15, seven new cases had developed, and the adoption that night of the measures of caution described above, and a policy of complete early isolation of all fever cases, apparently had the effect of preventing further contacts with the newly developing cases, and thus halting the flare-up. After that date, only three new cases developed, two of them direct contacts already under supervision, and the third an isolated case (Chart 6).

The other noteworthy feature of the Saugerties epidemic observable from the chart is the high proportion of cases definitely traced to contact with previous cases. Twenty-six cases were traced to six foci of infection, and in only sixteen out of the total of forty-nine cases — or one out of three — could no history of contact or source of the disease be obtained.

In other respects the Saugerties instance presented the fairly typical features of an outbreak of epidemic poliomyelitis, as regards:

(*a*) Attack rate — 5 per thousand population.

(*b*) Proportion of fatalities — 16 per cent.

(*c*) Age incidence — all known cases 10 years or younger.

(*d*) Duration of acute symptoms — in twenty-three cases, 3 to 7 days (of these, ten lasted but three days).

(*e*) Incubation period — in nine out of thirteen cases with complete histories, ten days or less; in no case over two weeks.

(*f*) Proportion of cases paralyzed — nearly half of reported cases (twenty-two out of forty-nine).

PERIOD OF INCUBATION AND INFECTIVITY

From the study of a large number of cases in which a single exposure could be determined, it may be stated that the incubation period of the disease varies from four to fourteen days, with an average of about a week.

The persons taken with the disease were found to be sources of active infection for a period of at least eight days after the onset. In a number of cases infection took place as short a period as two days before the frank onset of poliomyelitis symptoms. There has been little evidence, however, of the disease being contracted from a person who had been ill longer than two weeks, which suggests the limit of the necessary period of isolation to be required for suspected cases of poliomyelitis in future outbreaks.

INFANT WELFARE WORK IN WAR TIME *

GRACE L. MEIGS, M.D.
WASHINGTON, D. C.

At this time everyone is scrutinizing eagerly the experience of the foreign countries which have been at war for almost three years. In every branch of activity we are anxious that the experience of those countries shall be of service to us, in order that we may avoid the mistakes that have been made and pursue the lines of work that have proved to be successful.

In looking over the mass of material offered on such a subject as the question of what has been done in foreign countries for the protection of infancy and maternity since the war began, it is immediately evident that a great deal of the detail of the experience recorded is worthless to us, simply because the associated conditions in the foreign countries are very different from those in our country. In each country many factors in the past have influenced the development of measures for the protection of infancy and maternity; among them are varying industrial conditions and standards of living, different methods of organization of public health and social protection, different conditions as to high infant mortality rates and falling birth rates. The countries overtaken by the war in August, 1914, and since that time, had already traveled different lengths along the road toward complete protection of infancy and maternity, and in each country different methods had been developed. It may be said at once that it would be dangerous to accept without question a great deal of the foreign experience as applicable in this country.

The greatest value to us, in a study of such foreign material is to discover certain general tendencies for good which we can imitate, and certain general difficulties which we should avoid if we can.

I should like to sum up at once what I believe these general lessons are with regard to the protection of mothers and babies in war time, as shown by a brief study of foreign reports.

In every country, and most of all in those countries which are hardest pressed — such as France and Belgium — work for the protection of infancy and maternity has been greatly increased since the war began. The decrease in the birth rates, and the fear of an increase in infant mortality rates have contributed to this interest. Especially,

* Submitted for publication June 28, 1917.

* Read before the Section on Health, National Conference of Charities and Correction, Pittsburgh, June 9, 1917.

concern for the protection of maternity as being an indispensable part of any plan for the protection of infancy, has received a remarkable impetus since war broke out. This is perhaps the one most striking feature of the foreign reports.

Another striking point is the great and successful effort which has been made in most of the foreign countries to strengthen the preventive rather than the palliative side of infant welfare work; in other words, to insure good and intelligent care of the baby by a healthy mother in her own home, rather than to give care for infants in day nurseries or other institutions. This is a notable change, certainly, from the measures employed in the wars of other days. It is the fruit of the intelligent movement for the prevention of infant and maternal mortality carried on during the previous decades.

In most countries the government itself has taken an unwonted part in such protection of mothers and babies. The line of development has not usually been toward anything new, but has been toward the expansion of work and of methods whose value for that country had already been demonstrated.

On the other hand, certain difficulties are manifest also in every country, but most of all in those countries farthest removed from the war: First, the diversion of interest and of private support from the protection of infancy and maternity to work which has a more dramatic or urgent appeal; and second, the difficulty encountered in continuing and enlarging work for infant and maternal welfare when a large part of the medical and nursing professions are called into active military service.

The chief value to this country of the foreign reports lies in this evidence they give of the added interest in the welfare of mothers and babies felt in those countries hardest pressed by the war; and of the difficulties which have been met in carrying out measures for child welfare in the face of war conditions.

The question of the increased need for the protection of mothers and babies in war time is at present felt by many people in this country to be an academic one; among the host of more dramatic appeals put forth, each one of which is claimed to be the most important in the present crisis, this question is lost sight of. You know, perhaps, the story of a meeting of women called in a large city to consider war work for women. It was addressed by the Director of the Division of Child Hygiene of the City Department of Health, who spoke of the greater necessity for infant welfare work in war time. Her speech was greeted with perfunctory applause; immediately women began popping up all over the audience saying: "Madam President! Madam President! Was this meeting called to discuss the feeding of children

or preparations for war?" "I want to nurse wounded soldiers." "But what are we going to do for our country?"

This is an extremely natural tendency; but it is a dangerous one. If the experience of foreign countries is to teach us anything, it should teach us that it would be wise to realize the importance of protecting the children, even though an extremity of need does not at present force this realization; that early in the war is the time to preserve the integrity of our work for infant and maternal welfare, before that work is disorganized by the loss of physicians and nurses. As the war goes on, doubtless many especial problems will arise; if the already established work is disorganized these problems cannot be met.

And now I shall summarize briefly the experience of a number of the belligerent countries along these three lines:

1. The influence of the war on the public protection of mothers and babies through public health nursing and infant welfare stations; through prenatal care and proper obstetrical care.

2. The influence of the war on measures to insure financial aid during pregnancy and at confinement, thus making proper care possible.

3. The influence of the war on the protection of pregnant women and nursing mothers in industry.

While certain of the measures to be described are necessary or appropriate only in the country which has developed them, certain other measures have been proved successful in all countries alike. The first of these is the establishment of centers which we may call in general "infant welfare stations," though they bear different names in the various countries. At such centers women receive advice and direction in keeping their babies well. At many of them prenatal work is also carried on; prospective mothers are given instruction and advice in prenatal hygiene, as well as medical supervision and care. The second measure, whose worth has been proved in all countries, is the teaching of the care of the mother and the baby in the mother's own home by a woman especially trained to give this teaching. In the different countries she is called an "infant welfare or public health nurse," a "sister" or a "health visitor." The rapid development of such work for the welfare of mothers and babies in foreign countries in the decades before the war has been described by Phelps[1] and Holt.[2]

ENGLAND AND WALES

Among all the countries, the experience of England since the war began is especially interesting and valuable to this country.

1. Phelps, E. B.: The World-Wide Effort to Diminish Infant Mortality, Tr. Fifteenth Internat. Cong. on Hyg. and Demog., 1913, **6**, 132.

2. Holt, L. E.: Transactions of the American Association for Study and Prevention of Infant Mortality, 1913, **4**, 24.

In England the same urgency has not been lent to the question of protecting babies as that felt in France on account of the low birth rate. And yet, in England, practically from the first day of the war, extraordinary measures have been taken to maintain and increase all means looking to the protection of mothers and babies. The part played by the national government is perhaps the most salient point in this work.

It happened that just before the war parliament was considering a grant to aid local sanitary authorities and voluntary agencies in carrying out such plans for maternal and child welfare as were approved by the Local Government Board. The grants made yearly to such work might amount to one-half of its total expense. In a memorandum bearing the interesting date of July 30, 1914, the Local Government Board gave the details of what such schemes should include, divided into measures for antenatal, natal and postnatal care. The systematic home visiting of infants and young children was dwelt on, as well as the carrying on of centers for infant and maternal welfare. Especially emphasized also were the need of coordinating public and private work; the importance of providing proper prenatal and obstetrical care; and the desirability of giving greater attention to the care of the child between infancy and school age.

This grant before the war fortunately placed in the hands of the Local Government Board a powerful means for stimulating and helping work for infant and maternal welfare after war began; and the board has used it with great success. Throughout it has taken the stand that in war time, in spite of the general need for economy, no economy should be exercised in this direction. There is evidence that in a good many communities, on account of lack of money and private support, the authorities or voluntary agencies have been slow to increase their work, or to undertake new work. These difficulties the Local Government Board has largely overcome. It has gone on with the greatest determination towards its acknowledged goal — to have systematic supervision through the work of health visitors for all babies born who need care. It was estimated that to accomplish this, one full-time health visitor for every 500 births reported annually was necessary.[3] The passage, in 1915, of the Notification of Births Extension Act was a powerful help toward this end. Through this act the immediate notification of all births to the health authorities was made compulsory in all parts of the British Isles; this notification within thirty-six hours makes possible the immediate visiting of the mothers of all babies born who need care.

The Local Government Board has succeeded so well that in the reports of the board and of its medical officer, Sir Arthur Newsholme,

3. Rep. Grt. Brit. Local Govt. Bd.: Maternity and Child Welfare, 1916, p. 16.

for 1915-1916, the statement[4] could be made that health visitors were now employed or subsidized by all the metropolitan boroughs except Camberwell, and by all the county boroughs except Gateshead. While in March, 1914,[5] there were only 600 health visitors employed by local authorities, this number had increased to 812 at the end of 1915, and to about 1,000 (including full-time and part-time workers) in 1916. This represented one health visitor, approximately, to every 800 births annually.

The increase in work for the protection of maternity through the careful supervision of midwifery and the provision of free prenatal care and skilled confinement care for those unable to pay for it, is less easily shown by figures; but this increase is very manifest in the reports.

In addition, the extension of infant welfare work to all children up to school age has been a successful part of the campaign.

Summing up the work of the Local Government Board, Sir Arthur Newsholme makes this statement in his report for 1915-1916:[6]

> The war has had the effect of directing greatly increased attention to means for improving the health of mothers and their children during the first five years of life. During 1915 work with this object has been much increased, though some local authorities still remain inert, and appear to be unwilling to realize that the truest national economy can only be secured by saving life and improving health by all practicable means.

That the Local Government Board is planning still greater efforts is shown by recent press articles and by correspondence. Lord Rhondda, soon after his appointment as president of the board, declared it as his belief that the lives of 1,000 babies[7] could be saved each week. And now we hear that the board is taking an active part in carrying out a National Baby Week in July, 1917. There is a National Baby Week Council, of which the Prime Minister is president, and the president of the Local Government Board, chairman. The board is sending suggestions as to the campaign to mayors, medical officers of health and town clerks in 250 districts. It is estimated that 800 to 1,000 different campaigns will be held. The National Baby Week Campaign, like that in this country last year, is to be one of education.

Another branch of the government has also taken part in infant welfare work since the war began. This is the Board of Education,

4. Rep. Grt. Brit. Local Govt. Bd.: Forty-Fifth Annual Report for 1915-1916, Part 3, p. 13.

5. Grt. Brit. Local Govt. Bd.: Supp. containing Report of Medical Officer for 1915-1916, p. 34.

6. Grt. Brit. Local Govt. Bd.: Supp. containing Report of Medical Officer for 1915-1916, p. 4.

7. Editorial: The Times, London, April 2, 1917.

which offers grants in aid to schools for mothers and to day nurseries, and has set up standards for the work of the institutions receiving this aid.[8]

Such work as above described is educational; it is directed against one of those two primary causes of infant mortality, ignorance and poverty.

The forces affecting the economic conditions of the mothers and their babies are of course of primary importance. Conditions which enable a mother to provide herself with proper care during pregnancy and confinement, and which make it possible for her to nurse her baby and care for him in her own home are the most powerful agencies of all for maternal and infant welfare. We may say that just compensation to dependents of soldiers is, after all, the greatest war measure that can be taken for the preservation of infant life in the presence of war.

I shall not here discuss the relation of economic conditions in England since the war began to the welfare of mothers and babies. I do wish, however, to say a word on one phase of this question: that is, the maternity benefits under the National Insurance Act. Like most of the other countries in which some system of maternity insurance was in force at the outbreak of the war, Great Britain has continued this work during the war, in the face of some difficulty. In 1914 the health insurance fund was facing a deficit because of the unexpected high rate of sickness among married women; and £500,000 were appropriated by parliament to cover this deficit. In the following year £150,000 were appropriated for the same purpose.

From English reports we have been unable as yet to obtain any definite information as to the relation of the profound change brought about in industrial and economic conditions by the war to the employment of pregnant women and nursing mothers in factories, especially in munition factories. While the statement is made that many mothers of young children are being employed in factories, here, as in other countries, definite figures seem to be lacking to show whether this is actually the case.

England, like all foreign countries, is watching its infant mortality rate and birth rate with as much concern as its casualty rates. In England and Wales, as elsewhere, the birth rate has fallen markedly; the infant mortality rate, as giving evidence of the success or failure of all the measures spoken of, has been watched, therefore, with all the more eagerness; and to everyone's great satisfaction it reached in 1916 the figure of 91 per 1,000 births, the lowest for any year on

8. Grt. Brit. Bd. of Education: Annual Report of the Chief Medical Officer for 1915, p. 24.

record. This fall was not immediate, however; the rate for 1914 was about the same as that for the year previous (105 as compared with 108); that for 1915 rose slightly, being 110. The fall in 1916 has aroused enormous interest. It is attributed to many things. A comparatively cool summer no doubt played some part. To the increase in wages great importance is also ascribed. A great deal of the credit is given, and no doubt with justice, to the remarkable increase in the measures which have been taken to protect infancy and maternity.

SCOTLAND

In Scotland a good many of the same measures have been carried out as in England and Wales; and here, too, the infant mortality rate declined very markedly in 1916; 111 per 1,000 births in 1914, it rose to 126 in 1915, and then fell to 97 in 1916, which was 9 points less than the lowest record ever before recorded for Scotland.

GERMANY

Our knowledge of conditions in Germany is far less complete than of those in England. We have but little information covering the last year and a half.

I can best sum up the effect of the war on work for the protection of mothers and babies in Germany by quoting reports of Drs. Langstein and Rott, director and assistant at the Kaiserin Auguste Victoria Haus zur Bekämpfung der Saüglingssterblichkeit im Deutschen Reiche. This institution is the official headquarters of the movement for the protection of infancy in Germany. Their articles published in the early part of 1915 tell us only of conditions in the early months of the war; but they are interesting as showing the lines on which the work was laid out in Germany for the war period. Dr. Langstein[9] says:

> Certainly never was the truth of the saying that children are to be regarded as the most valuable capital of the state more clearly apparent to every one than at the beginning of the war. The greatest care of all those who were engaged in social work was the preservation of all those measures for the protection of children which Germany has established in the last few years, and which may serve as models, and to which we are primarily indebted for the fact that a decrease in the infant mortality rate has been attained.

Langstein speaks of the fact that in the early days of the war attention was directed primarily to care for the army and for the wounded. Nevertheless, very soon after the beginning of the war a meeting of representatives of infant welfare work in Berlin took place at the Reichstag. The resolution to continue infant welfare work and to

9. Langstein, L.: Die Bedeutung des Kriegszustandes für das Schicksal der Kinder. Ztschr. für Säuglingsschutz, 1915, **7,** 41.

increase it was expressed, and this resolution was communicated to other German communities. The effort has been successful. Langstein continues:

> As far as information is available, it may be said that the care of infants in Germany has shown in time of war on what a firm foundation it rests. The work, which was established in time of peace, has in general continued. The people who were in charge of the work have been conscious that it is just as important a patriotic task to serve children who need care as to serve the soldiers in the field. I have been informed, it is true, that in certain regions of East Prussia, evidently under the stress of a dread of hostile attacks which are continually recurring, the work for the protection of infants has been discontinued.

Langstein also speaks with regret of the closing of the Neumann clinic for children in Berlin.

A few months later, in June, 1915, Dr. Rott[10] reported on a questionnaire sent to officials and private organizations in over 375 communities of over 15,000 inhabitants, and to 788 infant welfare centers, to 266 institutions for the care of mothers and babies, and to 271 day nurseries. The object of this study was to find out the effect of the war on the great system of infant welfare work which had been developed in Germany before the war. Eighty-one per cent. of the communities answered the questionnaire. It was found that in only 2 per cent. of these communities had work decreased; in 10 per cent. it had increased, and in the remainder, 88 per cent., it had continued unimpaired. The centers which had been closed were those which depended on private subscription. The loss of physicians and nurses to war work was remarked on in many communities; especially characteristic of private associations was a tendency of the sisters who had been carrying on infant welfare work to leave it for active military duty. Dr. Rott described this tendency as unnecessary and deplorable. He says:

> The lack of physicians and nurses is to be regarded as a direct result of the war; the scarcity of the former may be considered, for the most part, as necessary and unavoidable; that of the nurses, however, is by no means unavoidable. It is certainly a deplorable fact that a large number of infant welfare sisters and attendants at the beginning of the war offered themselves for the care of the wounded (although in this department there was an oversupply of nurses), and so withdrew themselves from the extremely necessary infant welfare work.

One section of Dr. Langstein's report is especially significant.

> Extraordinarily interesting, and not foreseen by many was the fact that since war began less use has been made than in times of peace of asylums, especially of infants' homes, intended for the care of healthy infants, and also of day nurseries. People at first thought that this would be different; and many promi-

10. Rott: "Die Einwirkung des Krieges auf die Saüglingssterblichkeit und die Saüglingsschutzbewegung," Ztschr. für Saüglingsschutz, 1915, **7**, 177.

nent women were convinced that the need for asylums and day nurseries would be so great that the establishment of new ones was an urgent necessity. . . . An absolute need for the establishment of day nurseries and homes (*Krippen und Heimen*) did not exist, as the course of the war has taught; and I may say that this is the finest proof to what a high level the care of infancy has attained in at least a number of large cities.

Dr. Langstein goes on to say that this was not the case everywhere. In Vienna, for example, there were few institutions for the care of children; and here their rapid establishment in troubled times caused great difficulty.

The reason why certain day nurseries were little used was because the mother, now unemployed, was in the position to keep her child with her and to devote herself to its care. It seemed to many thoughtful people that to strengthen this bond, which the war has tied anew, was a task fine and important, not only for the present, but for the future.

Dr. Rott also speaks of the establishment of many day nurseries after the war began, because of the impression that women would go to work at once. Many remained unused because of the lack of employment for women; where the nurseries were used the results were bad, because of the fact that they were carried on with low standards as to space, equipment and personnel. "Happily, some of them were soon closed," he remarks. He is convinced of the benefit of offering a "stillprämium," or allowance to a mother who nurses her baby.

Both speak of the mistake which was made early in the war, when an appeal was made to rich families to undertake the support of children away from their mothers. Dr. Langstein says that, on the other hand,

It seemed to the discerning that the only way to meet the need was through strengthening the bond between mother and child, namely, by giving financial aid to the mother or to a good caretaker who desired to keep the child with her, but who was unable to do it on account of financial difficulty.

He says that this fact has been taken into account in Berlin by the special committee for the care of mothers and infants, which is part of the Red Cross. The committee stipulates that the mother shall bring her baby regularly to an infant welfare station. It is said:

This fund gives to all mothers, who are shown to be in need, and who during the course of the war wish to take care of their children in their own homes, a monthly allowance; and fulfils therewith a task which is not only successful as regards health, but is also a great social task. I hope that the work of this committee may not end with the peace which we hope will soon come.

Dr. Rott reviews other measures which have been taken which seem to him of paramount importance for the welfare of mothers and babies in Germany. First among these he speaks of the government provision made for the maintenance of families of soldiers, supplemented by the provision made by communities.

Secondly, he speaks of the *Reichswochenhilfe,* the maternity and nursing benefits now paid by the imperial government. The effect of the war on maternity insurance in Germany has been an interesting one. In August, 1914, the Reichstag, fearing the effect of the war on the solvency of the health insurance societies, curtailed greatly the maternity benefits. It soon became evident that the sickness insurance societies were less affected by the war than had been feared; also the need for the protection of wives and babies of soldiers seemed very great. Therefore the imperial government assumed the burden of maternity benefits for wives of soldiers who would not otherwise receive benefits, and these were increased over the benefits previously paid. The benefit paid for twelve weeks after confinement to mothers who nurse their babies was a special feature. Another act in 1915 still further increased the number of women to be benefited. The government is now expending 5,000,000 marks a month for this purpose.

No German reports have been available on the subject of the development of work for the protection of babies in Germany during the second year of the war. However, light is thrown on this question by the "Report on Milk Supply in Germany,"[11] prepared by Prof. A. E. Taylor of the American Embassy staff in Berlin in 1916. He finds no evidence that infants in Germany have suffered because of the decrease in the milk supply since the war began. Measures had been taken early to prevent any such hardship. It is said:

> The question of the adequacy of the supply of milk for the needs of the German empire was realized early in the war and regulations were promulgated by the authorities for the purpose of accurate control. The use of milk, apart from that applied to the making of cheese, was grouped under four headings:
>
> (*a*) Use of milk by the nursing mother and the weaned infant.
>
> (*b*) The use of milk by children from the second to the twelfth or fourteenth year.
>
> (*c*) The use of milk by the sick under the care of physicians.
>
> (*d*) The use of milk as a beverage by healthy adults.
>
> The use of milk as a beverage by healthy adults was regarded, under the conditions at present pertaining in the German Empire, as luxury; and it was ordered that no milk should be dispensed for this purpose until all requirements under the three first-named headings (*a, b, c*) had been fully supplied. The reduction in the milk supply has naturally been felt most keenly, and indeed almost entirely, in the cities, and in many cities in the empire there has been during the past winter little or no use of milk as a beverage by healthy adults.

As explaining the decline in the infant mortality rate during 1915 Professor Taylor says:

> This extremely favorable and impressive reduction in the death rate of children under 1 year was achieved through the cooperation of several agencies. It

11. Taylor, A. E.: Report on Milk Supply in Germany, U. S. Department of State, 1916.

is an axiom with workers in social service that the fewer the children the better the care which they receive; and this undoubtedly has held in Germany, particularly in view of the insistence placed by the press on the preservation of the future generation. Added to this was the fact that the summer of 1915 presented a subnormal mean of temperature, which, here as everywhere, operates to reduce the so-called intestinal diseases of infants. Lastly, the social service organizations in the cities of Germany have, during the past winter, reached a point of unequaled thoroughness and excellence. In the city of Berlin alone there are some 6,000 workers actively engaged in social service. Under these circumstances it has been possible to uncover and combat practically all instance of need in the care of infants. There is nowhere to be found any evidence of any reduction in the milk supplied to nursing mothers and infants in Germany during this period of time.

In Germany great attention has been given to the question of the effect of the war on the birth and infant mortality rates. The infant mortality rate for 1914—164 per 1,000 births—was a marked increase over the rate for 1913, which was 151 per 1,000 births. Dr. Langstein prophesied that this increase would probably be shown by the figures for 1914-1915 because of the prevalence of summer diarrhea among infants in August and September, 1914. This he ascribes to the hot summer and to the effect of the many conditions attendant on the breaking out of war.

The drop in the birth rate for 1915 showed markedly the effect of the war. The infant mortality rates, however, showed also a decrease, at least in the larger cities. Official reports for the infant mortality rates of 1915 and 1916 for the whole of Germany have not been available. The *Deutscher Reichsanzeiger*[12] reports an interesting official study which was made of the figures for births and infant deaths in the twenty-five large cities of over 200,000 inhabitants for the three months from August 1 to October 30, 1915. As compared with the same period of the year before, there was a decrease in the number of births of 15,457. The decrease in the number of deaths under one year was 6,354. The statement is made:

The decrease in the number of births was therefore almost one-half counterbalanced by the lowering of the infant mortality. . . . These relations would lead one to suppose that in general with the decrease in the number of live-born, an increase has occurred in the welfare work undertaken in certain cities; or that this work became more efficient because it reached better the infants needing help than when the number of infants was larger. It is true that the favorable weather conditions of the summer months of the year 1915 were in addition a favorable influence.

Dr. Taylor's report gives information on this point covering a later period in the second year of the war:

The *Kaiserl. Gesundheitsamt* keeps a special record of the death rate of children under 1 year. These figures are published up to January 1, and the unpublished figures up to April 1 have been kindly placed before me in the

12. Deutscher Reichsanzeiger, Feb. 8, 1916, No. 33.

Gesundheitsamt. They display, in a most striking manner, a reduction in the death rate, a reduction unparalleled in Germany in time of peace. In fact, viewing the figures as a whole, it is clear that the reduction in the death rate under the first year of life has been so large as to have compensated for half of the reduction in the birth rate during the past year.

FRANCE

In France the available reports deal chiefly with the work for maternal and infant welfare in Paris. This was organized early in August, 1914, with Paris under military government, with the title *Office central d'assistance maternelle et infantile.* The published program of this office was this:

> During the entire war, and in every part of the military government of Paris to assure to every woman who is pregnant, or who has a baby less than 3 years old, the social, legal and medical protection to which she has a right in a civilized society. To be sure that no woman is ignored and no child is forgotten.

Delegates of the office were installed in the eleven maternities of Paris of the *Assistance publique* (the official agency in charge of charities in Paris), to which most needy women come for confinement, and in the *mairies* to which they apply for medical assistance when they are confined at home. The object of this office was evidently to make the work already carried on immediately available to the women needing help; to stimulate all organizations and institutions to increase their work, and, where necessary, to establish new work.

Professor Pinard, in his reports on the protection of infancy in Paris during the first five months and during the first and second years of the war, has reviewed the measures taken. He says[13] that the medical protection of mothers before, at and after confinement, and of babies had never been so good in Paris as during the first five months of the war. The provision of free hospital beds for confinement was greatly increased; free consultation centers for pregnant women were established at every medical center. Military ambulances were provided to carry women to the hospitals. *Cantines maternelles* gave meals to pregnant women. The infant welfare stations or *gouttes de lait* continued their work. The lack of milk for babies who were bottle fed was at one time a great danger. This was obviated to some extent by the provision by the municipality of pure milk from the Paris herd especially for babies. About 12,000 liters of this milk were distributed daily. Pinard,[14] in later articles, reviews the measures which have been carried out by the government and the *Assistance*

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13. Pinard, A.: Bull. de l'Acad. de méd., Paris, 1915, **73,** 220.

14. Pinard, A.: Bull. de l'Acad. de méd., Paris, 1915, **74,** 343; ibid., 1916, **76,** 540. Pinard, A.: Ann. d'hyg. pub., 1917, **27,** 76.

publique in order to insure financial support for pregnant women and the mothers of young babies. These are:

1. The military allowance given to the mother of the children of soldiers whether legitimate or illegitimate.

2. The government maternity grant, which was established by the act of June 13, 1913.

3. The grant given by the government to large families.

4. The help distributed by the *Assistance publique,* and by the maternity hospitals, whose object is to enable the mother to care for her baby herself.

The degree to which the public provision for confinement care has been used seems the most astonishing fact in the figures given by Pinard; they reveal a need for economic assistance on the part of almost all the mothers confined, which creates a profound impression. While in 1913-1914, 78.5 per cent. of all the births in Paris were cared for either by the maternity hospitals of the *Assistance publique,* or through its medical service outside the hospitals, this figure rose in 1915-1916 to the astonishing percentage of 95.2 per cent. That is, in 1913-1914, 10,465 women out of 48,917 went through confinement in Paris without the help of the *Assistance publique;* in 1915-1916 only 1,250 out of 26,179. The figures show, too, the fall in the birth rate in Paris; in 1915-1916 the number of births was only a little more than one half what it was two years before, in 1913-1914 (48,917 in 1913-1914; 26,179 in 1915-1916).

The results of this work in Paris, Pinard sums up in his papers. The results for the first year from Aug. 1, 1914, to Aug. 1, 1915, were very encouraging. The infant mortality rate among the babies remaining in Paris declined; the maternal mortality rate fell as did the still-birth rate. The death rate under 2 years, however, remained about the same. There was a remarkable decrease in the number of babies put out to board outside of Paris. In 1913-1914, before the war, the number of children who did not have the benefit of their mother's care for this reason was 14,925; in 1914-1915 it was only 4,954. The percentage of new-born babies abandoned was considerably lower in the first year of the war than previously.

Dr. Pinard's report for the work during the second year of the war, Aug. 1, 1915, to Aug. 1, 1916, shows results no longer so encouraging. While the work described above was continued or was increased (the number of women helped at confinement now being 95.2 per cent. as has been said), the work was less successful in some respects, although the infant mortality rate among the babies remaining in Paris was still less in the second year of the war than in the first. There was, moreover, a decline in the mortality in the early months of life and from

diarrheal disease. The last named decrease Pinard attributes to the work done: (*a*) to protect babies before birth; (*b*) to insure in a larger number of cases that the mother should stay with her baby and nurse him; (*c*) to provide good milk when breast feeding was impossible.

On the other hand, the death rate of children under 2 years was higher than before the war. The rates from measles and whooping cough increased. Most disquieting to Pinard are the following facts as shown by the statistics of Paris for the second year of war. The percentage of new-born infants abandoned increased greatly, so that it was actually higher than before the war; also the number of babies put to board outside of Paris was much greater than in the first year, though still less than before the war. The stillbirth rate and the maternal mortality rate had also increased.

Pinard draws from these results conclusions which are destined to make his report a famous one, for they have given rise to a heated and protracted controversy. Pinard believes that the unfavorable results obtained in Paris during the second year of the war are only to be explained by the entrance of pregnant women and nursing mothers into industry in factories, especially munition factories. Pinard, therefore, at the meeting of the French Academy of Medicine, at which he had read his report, proposed that resolutions should be passed by the Academy advising the government to take the following measures: To forbid that any woman in France who is pregnant, nursing her baby or confined within six months should be employed in factory work; and that every French woman pregnant or nursing a baby of less than a year should receive on her demand, an allowance daily of 5 francs.

The discussion that arose in the Academy of Medicine over this speech of Pinard and the report of a committee appointed to consider it was continued at many of the weekly sessions from Dec. 5, 1916, until March 13, 1917.

It is evident that both sides in this controversy had equally at heart the same object: the protection of infancy and maternity in France; they differ greatly as to the method to be employed. One side favors abolition of factory work, especially in munition factories, for pregnant women and nursing mothers; the other side favors its regulation. One point seems clear on reading the reports of this discussion: there is little actual knowledge of whether or not the number of pregnant women and nursing mothers now employed in factories, especially munition factories, is actually as great as the conclusions of Pinard and his followers would lead one to suppose. The only evidence that is available tends to show that this number has been overestimated. M. Bonnaire reports that at the Maternité in one month, November 10 to December 10, 1916, 7 per cent. of the 445 women confined had been

working in munition factories. Most of these had, however, obtained a change of work or had stopped work because of their condition. One speaker, M. Bar, in the discussion at the Academy related the results of an informal investigation in a few big munition factories as to the number of women employed who were pregnant or had children under one year. He felt sure that evidence as to the number of pregnant women was undoubtedly incomplete. He concluded, however, that not more than 1 per cent. of the women working in these factories was pregnant, and not more than 2 to 3 per cent. of the women had children under 1 year.

During the discussion, the resolutions passed in December, 1916, by the committee on female labor appointed by the Ministry of Munitions regarding the protection of pregnant women in munition factories were discussed; these deal with the forbidding of night and overtime work, work in the last four weeks, and certain forms of labor to pregnant women; also with medical supervision of such women.

After prolonged debate, the resolutions of Pinard were defeated, and resolutions were passed by the Academy based on the report of the committee appointed. These resolutions embody still further recommendations as to the regulation of the work of pregnant women and nursing mothers in munition factories, and in order to favor maternal nursing advise the establishment in factories and munition factories of rooms where working mothers can nurse their babies.

The latter institutions were especially discussed during the debate. Pinard said that while he had sometimes favored their establishment, that he considered them very difficult to manage well. He knew of only one which was satisfactorily equipped and conducted, and that was carried out at a high cost, estimated at about 5 francs a day per child. Lesage, in numerous publications, has urged the establishment of these rooms in munition factories, and has emphasized the great precautions which must be taken in carrying them on.

BELGIUM

About the work for maternal and infant welfare in Belgium, Dr. Lucas'[15] report gives us immensely interesting information.

Information as to death rates is of course difficult to secure in Belgium, but all the figures available point to an actual decrease in the infant mortality rate in at least the large cities of Belgium (with the exception of Mons) since the beginning of the war.

Dr. Lucas writes:

> General solicitude for the children has resulted in an actual improvement in infant conditions to a point above the normal. . . . It is generally evident that

15. Lucas, W. P.: General Health Conditions in Belgium After Two Years of Relief Work, Jour. Am. Med. Assn., 1917, **68**, 27.

infant conditions are on the whole better than normal, that class having been the object of great solicitude since the beginning of the war. A great many institutions have been created during the war to care for the children. The organization of the work for the children has been divided into canteens:

1. Canteens for nursing and expectant mothers. . . . There are over 13,000 nursing and expectant mothers receiving these dinners.

2. Canteens, often in conjunction with maternal canteens, have been instituted for infants under 3 years, in which there are over 52,000 infants receiving milk and cereals.

Both these types of canteens have undoubtedly had a great influence on the reduction of infant mortality in Belgium. There is no question that today, in Belgium, more is being done for the mother and the child than was ever done before. Previous to the war there were only two maternal canteens in the whole of Belgium; today there are over 329 canteens for infants. These canteens, in connection with the educational work, the medical supervision which all the canteens have, and the careful regulation of the dietary, both in the canteens and by an extensive system of visiting nurses, in the homes, have undoubtedly had a marked effect on this great reduction in infant mortality.

The fact that the educational and preventive work of these canteens has been made so marked a feature in the face of conditions such as those present in Belgium is, I believe, one of the greatest triumphs of preventive infant welfare work that can be thought of.

There is not space to speak here of work in Italy and Russia; moreover, our information about these countries is meager.

The experience of such countries as New Zealand and Canada is interesting to us in many ways, especially because their situation, far removed from the actual scene of the war, resembles that of this country. In these countries, from the small amount of evidence at hand, it would seem that there has been no such increase in the care for the protection of maternity and infancy as that which has occurred in the countries already spoken of. On the other hand, there is much evidence that the work has suffered greatly from the loss of physicians and nurses called to active military duty.

In the report published in 1915 of the New Zealand Society for the Health of Women and Children,[16] which has done such remarkable work, we read:

While each individual member of the society and each Plunket nurse has been working more strenuously, the society has temporarily limited the sphere of its operations as regards the establishment of new residential centers for Plunket nurses. In some districts where sufficient funds had been collected to enable the local committees to apply for the government grant of 24 shillings for each pound subscribed, the Central Council asked them to hold the matter over in the meantime, and to work quietly without a Plunket nurse, getting an occasional visit from the nearest nurse as a stimulus to continued effort. This was done at the request of the government, in view of the greatly increased public expenditure which the war was involving.

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16. The Society for the Health of Women and Children, Eighth Annual Report, 1915, p. 3.

And in the report[17] published in 1916 it is said:

During the year a great many of our nurses who volunteered for war service left for the front, and several of the branches have been obliged to avail themselves temporarily of the services of Karitane nurses while new Plunket nurses were being trained. As arranged with the government authorities when war broke out, no new residential centers for Plunket nurses have been created during the year.

From Canada the reports of the Victorian Order of Nurses gives us an indication of the effect of the war on the work of this society which carries on infant welfare and prenatal nursing in connection with general public health nursing, not only in the large cities, but in the most isolated rural districts of the vast stretches of western Canada.

In her report for 1915[18] the chief superintendent, Miss Mackenzie, says:

The war has affected the order in several ways—our increases are not as great, and we have not opened up new districts in cities, many of which were ready to organize when the war broke out. In many of these districts the order is being used and appreciated more than ever before, and doubtless that will be still more noticeable as time goes on.

During 1915 twenty-eight of the band of 292 nurses of the order doing active work resigned to go overseas for war duty.

The 1916 report describes especially the effect of the war on the movement for public health nursing, especially maternity and infant welfare nursing in the isolated western country districts. This movement received a great impetus in 1912 through the establishment of the Duchess of Connaught's fund for nursing in new and sparsely settled districts. The report says:[19]

A promising beginning was made, but since the war came on us, it has become harder and harder to secure nurses for these outposts, and many districts ready to receive nurses have had to go without them.

Miss Mackenzie writes in general, however, that conditions are now better than the year before. She speaks of the shortage of nurses as one of the most serious handicaps, but says that this is gradually improving. In spite of this shortage she says: "The most gratifying development in the Victorian Order during 1916 is to be found in the country scheme." She writes also:

When the war broke out many of our committees were more or less panicky, fearing that it would be necessary to suspend V. N. O. activities until after the war, and town districts where branches were to have been organized

17. The Royal New Zealand Society for the Health of Women and Children, Annual Report, 1916, p. 6.

18. Victorian Order of Nurses for Canada, Report of the Board of Governors for 1915, p. 13.

19. Victorian Order of Nurses for Canada, Report of the Board of Governors for 1916, p. 14.

dropped all plans for the time being. Now, the past year has shown a wonderful change; the panicky condition is not noticeable at all, and the reports, with very few exceptions, show increased visits, increased fees and contributions.

She speaks of an increase in the work for infant and prenatal nursing.

Canada has given evidence of its interest in infant welfare through its Baby Weeks. The Children's Bureau last year had reports of three successful celebrations in Canada; and this year has heard of plans in seventeen cities, including large cities such as Montreal, Hamilton and Calgary, as well as small settlements in the far west.

Canada has shown a far-sighted liberality in its provisions for soldiers' families. These are described in Mr. Paul Kellogg's articles in the *Survey*,[20] and in a report by Mr. Wolfe recently published by the Children's Bureau.[21]

CONCLUSIONS

To me, as I have said, this brief study of how war has effected the protection of maternity and infancy in many countries seems to give us in this country some practical suggestions now that the United States is also involved in the war. These are:

1. No hasty conclusions should be drawn that the war makes immediately indispensable in this country such palliative measures as the increase of day nurseries or the supervision of pregnant women working in factories, to which dire necessity has driven certain foreign countries. Study is necessary to show how present and future economic and industrial conditions will affect the number of pregnant women and of mothers of young children employed in factories; and what measures are needed under these conditions.

2. The chief preventive measure for protecting babies is to insure their intelligent care and nursing by healthy mothers in their own homes.

3. The disorganization of infant welfare work through the loss of physicians and nurses especially trained for it, is an imminent danger, and should be avoided if it can be done. In view of the greater demand for nurses, every effort should be made to enlist a large number of candidates for hospital training courses.

4. The preventive work for infant and maternal welfare, already established, should be strengthened and extended; and nothing should be considered more important in war time.

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20. Kellogg, P.: A Canadian City in War Time, The Survey, 1917, **37,** 677, 709 and 739.

21. Wolfe, S. H.: Care of Dependents of Enlisted Men in Canada, U. S. Children's Bureau, Pub. 25.

THE URIC ACID CONTENT OF THE BLOOD IN THE NEW-BORN *

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It has long been known that the uric acid excretion in the urine of children during the first few days of life is both relatively and absolutely high. Reusing[1] determined the daily excretion of this substance during the first seven days of life of six normal children and found that it reached its maximum of 0.083 gm. on the third day. He used the analytical method of Gowland Hopkins.[2] Schloss and Crawford,[3] using the procedure of Folin and Shaffer,[4] determined the uric acid excretion of nine infants each day up to and including the ninth day, and found in four of the cases that the excretion reached its maximum on the third day; in two cases on the second day; in two cases on the first day, and in one case on the fourth day. Their results are confirmatory of Reusing's. Schloss and Crawford also pointed out that the urinary excretion of phosphorus was highest during the first three days of life and believed that this indicated a common source of origin of phosphoric acid and uric acid, the nucleoproteins. They did not, however, determine the fecal phosphoric acid excretion. The purin content of the colostrum they found to be too slight to account for the high uric acid excretion.

It is well known that during this period when the uric acid excretion is highest, rapid morphologic changes occur in the blood of the new-born. The disappearance of the nuclei of many of the red cells, the change in proportion from a predominating number of polymorpho-

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* A preliminary report of this work was made at the annual meeting of the Federation of American Societies for Experimental Biology, December, 1916, in New York City.

* Read at the meeting of the American Pediatric Society, White Sulphur Springs, W. Va., May 28, 1917.

1. Reusing, H.: Ztschr. f. Geburtsh., 1895, **33**, 36.
2. Hopkins, F. G.: Guy's Hosp. Rep., 1891, p. 299.
3. Schloss, O. M., and Crawford, J. L.: Am. Jour. Dis. Child., 1911, **1**, 203.
4. Folin, O., and Shaffer, P. A.: Ztschr. f. physiol. Chem., 1901, **32**, 552.

nuclear neutrophilic cells to a corresponding predominance of lymphocytes (Carstanjen[5]), and the striking decrease in the leukocyte count of the peripheral blood, are confirmed by Schloss and Crawford. These investigators refer to the work of Goldscheider and Jacob,[6] Schulz,[7] and Bohland[8] as evidence that the fall in the leukocyte count in the peripheral blood may not be due to an actual destruction of these cells, but to a redistribution, and therefore regard this question as unsettled as yet. It should be remembered, however, as pointed out by Von Reuss,[9] that the blood cell count is very much higher during the first day than during the latter days. That is, it is higher then than during the following days when the birthweight, and correspondingly the water content of the first day, has not yet been regained. The pigment content of the intestinal discharges, and perhaps the icterus neonatorum, as well as the leukocytic destruction of the uric acid infarcts and the increased uric acid excretion, may be considered as an expression of this process.

That the increased excretion of uric acid following the increased metabolism of nucleoprotein is so well known that it is unnecessary to refer to the large literature on this subject. This fact makes attractive the view that the increased excretion of uric acid in the urine of the new-born is due, in part at least, to a destruction of leukocytes at this time, but as already noted, the fact of such a destruction seems at present to be disputed. The cause of this increase in the uric acid output must, in the light of our present knowledge, be referred in part, at least, to an increased metabolism of nucleoprotein material; but just where in the body this is taking place must be regarded as an unsettled question.

The occurrence of uric acid infarcts in the form of neutral, acid ammonium urate or a mixture of neutral and acid ammonium urate in the kidney of the new-born during the first few days of life is an established fact, and it was shown by Schloss and Crawford that uric acid infarct elements were present in all the urines of the new-born in the cases already referred to.

The purpose of the present investigation is to determine whether or not the high uric acid excretion during the first few days of life is accompanied by a simultaneous increase of this substance in the blood. While it seemed probable that this would be found to be the case, there was, nevertheless, a reasonable doubt concerning this question

5. Carstanjen, M.: Jahrb. f. Kinderh., 1900, **52,** 215.
6. Goldscheider and Jacob: Ztschr. f. klin. Med., 1894, **98,** 373.
7. Schulz: Deutsch. Arch. f. klin. Med., 1893, **51,** 234.
8. Bohland, H.: Centralbl. f. inn. Med., 1899, **20,** 361.
9. Von Reuss: Krankheiten der Neugeborenen, 1914, Springer, Berlin.

which could be settled only by actual determination of the uric acid content of the blood.

METHODS

Benedict's[10] modification of the original Folin-Denis[11] method for the determination of uric acid was tried, but found more tedious than the later codification of Myers, Fine and Lough.[12] The latter modification, with certain minor changes,[13] was used throughout the work. By this means it was always possible to obtain an unknown blue solution that was perfectly clear and easy to compare with the standard. The standard color was that made by 0.4 mg. of uric acid, and was usually diluted to 30 c.c., a dilution that gave the most satisfactory depth of color when the colorimeter was set at 20 mm. The unknown color was diluted to the volume that gave approximately the same shade as the diluted standard, the regular procedure of Myers, Fine and Lough, and much more satisfactory in our hands than the older procedure in which the dilution was more or less arbitrarily fixed, with the result that one had frequently to compare colors that were of much greater degrees of difference and therefore harder to work with.

It was noticed by Curtman and Freed[14] that Benedict's[15] standard uric acid solution slowly deteriorated, and at the end of two months was no longer standard. This is confirmed by our experience. It was customary to check the standard solution from time to time against a new solution. It was found that the standard would hold its strength for at least ten days, but that while some solutions kept for a month or more, it was unsafe to assume that a standard more than ten days old was still serviceable.

Daylight was used wherever possible in reading the colorimeter, but in a few cases this was impossible without letting the analysis stand over at some stage until the next day. While there is no evidence at our disposal that indicates that a delay in the analytical procedure vitiates the results, it nevertheless happened that in most of the few cases in which no color was obtained with the uric acid reagent, the analysis had been delayed. As to the cause of these failures, which have been previously noted by Morris,[16] we have no definite information. In order to avoid this possible source of failure it was customary to use an artificial source of light in a few analyses. This consisted

10. Benedict, S. R.: Jour. Biol. Chem., 1915, **20,** 629.
11. Folin, O., and Denis, W.: Jour. Biol. Chem., 1912, **13,** 469.
12. Myers, V. C., Fine, M. S., and Lough, W. G.: Arch. Int. Med., 1916, **17,** 570.
13. Kingsbury, F. B., and Sedgwick, J. P.: Jour. Biol. Chem., July, 1917.
14. Curtman, L. G., and Freed, M.: Jour. Biol. Chem., 1916, **28,** 89.
15. Benedict, S. R., and Hitchcock, E. H.: Jour. Biol. Chem., 1915, **20,** 623.
16. Morris, J. L.: Jour. Biol. Chem., 1916, **25,** 205.

in a 100 watt nitrogen burner of "Daylite" glass enclosed in a box having a ground glass window. It was found that pure uric acid solutions gave the same relative colorimetric readings with this light as with daylight, and that it was fully as easy to compare the colors accurately. The blue solutions produced by the uric acid of blood, however, gave readings about 0.2 mm. higher than when compared with the same standard (at 20 mm.) under exactly the same conditions with daylight. For this reason the artificial light was used only when absolutely necessary to avoid letting the analysis stand over until the next day. Not more than ten colorimetric readings in the whole number of analyses recorded in this paper were made with this light.

COLLECTION OF BLOOD SAMPLES

Blood was drawn through a sterile hypodermic needle from the superior longitudinal sinus of the new-born into a glass syringe and

TABLE 1.—Determination of Uric Acid in Maternal and Placental Blood

Name	Maternal Blood, Uric Acid in 100 Gm. of Blood, Mg.*	Placental Blood, Uric Acid in 100 Gm. of Blood, Mg.	Name	Maternal Blood, Uric Acid in 100 Gm. of Blood, Mg.*	Placental Blood, Uric Acid in 100 Gm. of Blood, Mg.
Beau.	...	2.9	Wal.	3.1	3.2
Drey.	3.5	2.8	Han.	2.8	2.6
Pel.	3.6	3.3	Dahl.	2.9	3.1
McH.	2.2	2.4	Hus.	2.1	2.5
Ne.	2.9	2.7	Wes.	3.3	...
Mill.	3.1	2.8	Van.	...	3.1
Roos.	3.1	3.5	Aas.	2.1	2.3
Kr.	2.7	...	Swan.	3.7	4.1
Thom.	3.3	2.8		—	—
Han.	5.0	5.0	Average	3.1	3.1

* All figures are in milligrams per 100 gm. of blood.

expelled with force into a small weighing bottle containing 0.1 gm. of potassium oxalate.

The weights of blood samples used in the analyses recorded in this paper varied from about 9 to 18 gm., but the usual sample, particularly of infant blood, was about 13 to 14 gm.

Placental blood was collected as soon as possible after cutting the cord, which was done late, that is, after the cord had stopped pulsating. This blood, and also that of the mother, was also collected in weighing bottles containing 0.1 gm. of potassium oxalate. The maternal blood was drawn from a vein in the arm of the mother at the

TABLE 2.—Uric Acid Content of Blood of New-Born

Date of Birth	Sex	Name	Uric Acid in Placental Blood, Mg.	Uric Acid 0 to 23 Hours after Birth, Mg.	Uric Acid 24 to 47 Hours after Birth, Mg.	Uric Acid 48 to 71 Hours after Birth, Mg.	Uric Acid 72 to 95 Hours after Birth, Mg.	Uric Acid 96 to 119 Hours after Birth, Mg.	Uric Acid 5 to 8 Days after Birth, Mg.	Uric Acid 8 to 10 Days after Birth, Mg.	Weight New Born, Gm.	Water Given	Remarks
11/27/16	♂	Men.	9 hrs.	9 hrs. 4.2	....	....	....	....	....	....	3,445	—	1
12/ 3/16	♀	Hoff.	....	....	26 hrs. 3.7	....	....	....	....	....	3,340	*	2
12/ 4/16	♀	Kah.	....	23 hrs. 2.9	....	....	....	....	....	....	4,140	—	3
12/ 6/16	♂	Mart.	....	8 hrs. 4.9	....	....	....	....	....	10 days 1.3	3,445	*	4
12/11/16	♂	Kitt.	1.7	9 hrs. 2.7	....	....	....	....	....	....	3,120	*	5
12/ 9/16	♀	Rick.	3.1	....	....	....	....	96 hrs. 3.7	....	....	3,600	—	6
12/10/16	♂	Kenn.	1.9	....	46 hrs. 4.0	....	....	....	....	9 days 3.5	3,375	—	7
12/16/16	♂	Boye.	3.6	....	46 hrs. 3.8	....	....	....	....	....	2,280	*	8 †
12/19/16	♂	Schim.	2.8	....	44 hrs. 3.0	....	....	....	....	....	2,900	*	9
12/16/16	♂	Berl.	....	....	....	....	....	....	120 hrs. 2.1	....	3,375	—	10 ‡
12/16/16	♀	Berl.	....	....	....	....	....	....	120 hrs. 3.4	....	3,230	—	11
1/21/17	♂	McDon.	....	....	39 hrs. 5.1	....	....	....	....	....	4,060	—	12
1/20/17	♂	Ban.	4.3	....	....	....	72 hrs. 4.1	....	....	....	3,280	*	13
1/26/17	♂	Mel.	3.1	....	....	....	72 hrs. 4.2	....	....	....	3,930	*	14
2/ 1/17	♂	Spre.	....	23 hrs. 2.9	....	....	....	....	....	....	3,160	*	15
2/ 7/17	♀	Eich.	2.1	....	36 hrs. 3.6	....	....	....	....	8 days 1.7	2,740	*	16
2/ 9/17	♀	Thomp.	2.5	....	....	....	....	96 hrs. 2.6	....	8 days 1.4	3,160	*	17
2/ 9/17	♂	Mor.	2.7	....	....	....	....	....	120 hrs. 2.5	8 days 1.1	3,190	*	18
3/20/17	♂	Lars.	....	....	....	....	72 hrs. 3.8	....	....	....	3,220	—	19
		Dahl.	....	....	....	....	72 hrs. 2.8	....	....	....	.....	..	20
3/24/17	♂	Hol.	....	....	....	48 hrs. 4.5	....	....	....	....	3,650	*	21
3/24/17	♀	Sav.	....	....	....	48 hrs. 4.7	....	....	....	....	3,348	—	22
3/28/17	♂	Aas.	....	....	....	48 hrs. 2.5	....	....	....	....	3,750	*	23
4/ 1/17	♀	Zimm.	....	....	38 hrs. 3.7	....	....	....	....	11 days 1.1	3,420	*	24
4/ 1/17	♂	Peter	....	....	36 hrs. 3.0	....	....	....	....	....	3,910	—	25
4/ 4/17	♀	Hard.	....	....	....	48 hrs. 3.7	....	....	....	10 days 1.4	2,780	*	26 §
3/29/17	♂	Buhl.	....	....	....	....	....	....	....	10 days 1.5	2,870	—	27
4/ 7/17	♀	Smi.	....	....	....	....	72 hrs. 2.7	....	134 hrs. 3.4	....	3,330	—	28
4/ 7/17	♀	Math.	....	....	....	65 hrs. 3.4	....	....	....	....	3,020	*	29
4/ 6/17	♂	David	....	....	....	....	72 hrs. 2.9	....	....	....	4,220	—	30
	♂	Peter	....	....	....	....	72 hrs. 3.7	....	....	....	.....	..	31

time of parturition. All the new-born which served as subjects in this investigation were normal.

URIC ACID CONTENT OF MATERNAL AND PLACENTAL BLOOD

A separate series of analyses were made to determine the uric acid in maternal and placental blood in order to obtain a basis of comparison for the uric acid content of new-born blood. Several of the analyses recorded in this series had been made when it was learned that Dr. J. M. Slemons, of New Haven, Connecticut, was working on the placental blood as a separate problem. In a private communication he clearly established his priority in this matter and also reported that he had found identical values for the uric acid content of maternal

TABLE 3.—Average Values for Blood Uric Acid Each Day from Birth to Fifth Day

Age	Uric Acid per 100 gm. of Blood, Mg.	Number of Analyses on Which Average is Made
At birth*	3.0	42
0 to 23 hours	3.5	5
23 to 47 hours	3.6	8
48 to 71 hours	3.9	5
72 to 95 hours	3.5	7
96 to 119 hours	3.2	2
120 to 134 hours	2.9	4
8 to 11 days	1.6	8

* This is the average value for all maternal and placental figures.

and placental blood. His figures have not yet been published, nor are they known to us.

Our figures for this series of analyses are shown in Table 1. It will be noted that the average values for sixteen determinations of the uric acid content of maternal and placental blood are identical, agreeing in this respect with the independent finding of Slemons.

Table 2 shows the results obtained with the new-born. In some cases the infants were given water (marked * in the table) in addition to their ordinary diet of breast milk. It will be noted that the content of uric acid in the blood the first three or four days after birth is higher than that of the blood of the same new-born at birth. In seven cases there is a marked decrease in this value at the end of eight to eleven days from the value obtained (in each case with the same infant) three to eight days earlier.

Table 3 shows the average values for blood uric acid each day of life from birth to the fifth day, and during the period of the eighth to the eleventh day. It will be noted that during the period between the second and third days (forty-eight to seventy-one hours) the value reaches a maximum. A much larger series of analyses would be necessary to fix beyond question the day on which this maximum average value is reached; if, on account of individual variations, this could be established at all. During the first three or four days of life this value is higher than the maternal and placental figures.

From a maximum of 3.9 mg., the blood uric acid falls off slowly to 2.9 mg. on the fifth day and then rapidly to 1.6 mg. by the eighth to eleventh day. This value agrees with the 1.3 to 1.7 mg. found by Liefmann[17] in the blood of thriving children from nine weeks to fourteen months of age, on a pure milk diet.

CONCLUSION

Our finding that there is a parallelism between the high uric acid content of the blood of the new-born and the high excretion of this substance during the first three or four days of life, is indirect evidence supporting the findings of Wells and Corper[18] and others (in opposition to the results of Schittenhelm and Schmidt[19]) that human fetal tissues possess no uricolytic power, for it would be difficult to imagine so great a production of uric acid if the tissues themselves possessed the power to destroy it. Whether the decomposition of nuclein material, which must be looked on as the cause of this uric acid increase in the blood, is related to the striking changes in the blood cells, particularly in the changes in the partition of the white corpuscles taking place at this time, or to nuclein destruction in other parts of the body, as yet unknown, or to both, must be left to the future to decide. These results fit in well, however, as the connecting link in the theoretical chain of early leukocytosis — fall in leukocytes — *flood of uric acid in the blood* — high uric acid excretion — uric acid infarcts.

We wish to thank the members of the Graduate School in the pediatric department for obtaining for us the new-born blood samples, and also the members of the obstetric staff of the University for obtaining the samples of maternal and placental blood.

Syndicate Building.

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THE EFFECT ON HUMAN MILK PRODUCTION OF DIETS CONTAINING VARIOUS FORMS AND QUANTITIES OF PROTEIN *

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DETROIT

The problem of constructing a diet for a mother with a failing or deficient milk supply is one of the most difficult which is presented to the pediatrist.

The laity have any number of suggestions as to foods necessary; the physician has his favorite galactogogues; the nostrum vender advertises his wares as infallible milk producers, but in spite of all of these many mothers who begin nursing their babies soon find that their babies do not thrive on the milk which they are able to produce, and though they make a desperate effort to continue breast feeding they in time fail and their babies half starved, with resistance greatly lowered, are turned over to the pediatrist to feed on some form of artificial feeding.

The literature is practically barren of any extended researches on the effect of the diet on human milk production, but several excellent pieces of work have been done on milk production of the lower animals.

Voit contributed a valuable research on a bitch.[1] The animal was fed on meat alone, meat and fat, meat and starch, starch alone, fat alone and was also starved. Professor Lusk, in summing up the result of the experiment concludes that the influence on the milk secretion was found to be comparatively small.[2] Professor Lusk studied this problem as it related itself to the fat of goat's milk. He found that starvation greatly increased the fat content of the milk which returned to its normal level when the diet was resumed.

A most illuminating piece of work has been done to increase the production of milk in dairy cows. Under the direction of F. W. Wall, E. B. Hart and G. C. Humphrey of the University of Wisconsin, much scientific data on the proper feeding of cows for milk production has been obtained and published. The economic aspect of the problem has caused them to study particularly the nutritive ratio best adapted

* Submitted for publication May 28, 1917.
* Read at the meeting of the American Pediatric Society, White Sulphur Springs, W. Va., May 28, 1917.

1. Voit: Ztschr. f. biol., 1896, 137.
2. Lusk: Science of Nutrition, 1909, p. 235.

to milk production. Hart and Humphrey, discussing this question, state that "since the time of Wolff the feeding of cows has called for a narrow nutritive ratio; that is, a high percentage of digestible proteins in the ration. The ratios vary in proportion of digestible proteins to digestible fats and carbohydrates from 1:4.5 to 1:8.5.

Not only has the quantity of the protein most suitable for milk production in cows been studied by Hart and Humphrey, but also the quality of the protein.[3] Their findings are interesting and are summed up by them as follows:

"It was found that milk proteins had an efficiency for milk production and tissue reservation of about 60 per cent., while corn and wheat grain protein showed an efficiency of 40 and 36 per cent., respectively."

Believing that the determination of these same facts as regards human milk production would be of great value in establishing a proper basis for arriving at efficient diets, this work was undertaken.

Through the cooperation of the Detroit Wet Nurses Bureau connected with the Woman's Hospital and Infants' Home, suitable healthy mothers were placed under observation.

The food was all weighed. All the urine and feces collected. The breast milk was expressed by hand and accurately measured. The water intake was recorded. The daily weight of the mothers was kept. The total nitrogen was determined on the daily urine and milk output, and on the mixed food and feces for each period. The periods were five days each with the exception of one or two which were closed at the end of the fourth day.

The diets were carefully constructed from tabulated analysis made by Atwater and Bryant.[4]

The diets used were made to vary from a narrow nutritive ratio, that is, 1:4 to a very wide nutritive ratio, that is, 1:15. These ratios refer to the proportion of digestible protein to digestible carbohydrates and fats, the latter reduced to a cardohydrate basis.

Not only were diets with varying ratios used, but diets were also fed in which different types of protein predominated: In certain diets meat protein was used, in others, milk, cereal and nut protein. Some of these diets were high in calories, others, medium and low.

The diets may be characterized as follows:

Diet No. 1: Calories 3,767; nutritive ratio 1:5; fat to carbohydrate 3:2, predominating in animal protein, especially milk. Sources of protein as follows: milk 33 per cent., meat 21.5 per cent., cereal 33.5 per cent., vegetable 11.5 per cent.

Diet No. 2: Calories 3,446; nutritive ration 1:8; fat to carbohydrate 2:3, animal and vegetable protein in equal quantities: meat 27.7 per cent., milk

3. Hart and Humphrey: Jour. Biol. Chem., **302,**

4. Atwater and Bryant: U. S. Dept. Agriculture, Bull. 28,

14.5 per cent., eggs 8.5 per cent., vegetable 19.8 per cent., cereals 18.1 per cent., nuts 9.4 per cent., fruits 2 per cent.

Diet No. 3: Calories 3,503; nutritive ratio 1:9; fat to carbohydrate 1:4; vegetable protein entirely with exception of milk: cereal 60.5 per cent., vegetables 14.2 per cent., fruit 1.4 per cent., milk 23.9 per cent.

Diet No. 4: Calories 3,634; nutritive ratio 1:15; fat to carbohydrate 2:1; animal and vegetable protein in equal quantities, as follows: milk 37.1 per cent., meat 10.5 per cent., cereals 28.3 per cent., vegetable 18.6 per cent., nuts 5.6 per cent.

TABLE 1.—Diet 9

Food	Amount	Food	Amount
Oatmeal	150 gm.	Cocoa	4 gm.
Bread	200 gm.	Apple sauce	50 gm.
Butter	25 gm.	Lima beans	100 gm.
Round steak	150 gm.	Sugar	50 gm.
Eggs	100 gm.	Cream 20%	100 gm.
Potatoes	200 gm.	Spinach, squash or carrots	100 gm.
Milk	500 gm.	Hypophosphites	½ oz. three times a day before meals
Rice custard	100 gm.		

This diet approximated 2,927 calories. It contained 130 gm. of protein, yielding 20.64 gm. of nitrogen. The sources of the protein were as follows: meat 40.5 per cent., milk 15.7 per cent., eggs 10.5 per cent., cereal 21.2 per cent., vegetables 12.1 per cent.

Diet No. 5: Calories 2,088; nutritive ratio 1:9; fat to carbohydrate 1:1; animal protein diet, meat predominating: meat 32.9 per cent., eggs 12.9 per cent., vegetable 19.8 per cent., cereals 14.8 per cent.

Diet No. 6: Calories 2,774; nutritive ratio 1:6; fat to carbohydrate 3:2; animal protein predominating: meat 40.5 per cent., milk 15.7 per cent., eggs 10.5 per cent., cereal 21.2 per cent., vegetable 12.1 per cent.

Diet No. 7: Calories 2,842; nutritive ratio 1:5; fat to carbohydrate 1:1; animal protein predominating: meat 40.5 per cent., milk 15.7 per cent., eggs 10.5 per cent., cereal 21.2 per cent., vegetable 12.1 per cent.

TABLE 2.—Nut Diet 10

Food	Amount	Food	Amount
Malted nuts	100 gm.	Chocolate	8 gm.
Protose (nut product)	150 gm.	Bread	200 gm.
Pecans	25 gm.	Potatoes	200 gm.
Almonds	25 gm.	Lima beans	100 gm.
Walnuts	25 gm.	Peas	200 gm.
Peanut butter	50 gm.	Bananas	100 gm.
Cocoa	8 gm.	Apple sauce	50 gm.

This diet contained approximately 2,670 calories. The ratio of protein to fat and carbohydrate (all reduced to basis of calories) was 1:5. The actual number of grams of protein ingested was 104.68, yielding 16.75 gm. of nitrogen. Of this intake, 89 per cent. was absorbed. The mothers took the diet readily and enjoyed it.

Diet No. 8: Calories 2,286; nutritive ratio 1:13; fat to carbohydrate 1:4; pure vegetable protein: cereal 54.2 per cent., vegetable 40.3 per cent., fruit 5.5 per cent.

Diet No. 9: Calories 2,927; nutritive ratio 1:4; fat to carbohydrate 1:1; animal protein predominating: meat 40.5 per cent., milk 15.7 per cent., eggs 10.5 per cent., cereal 21.2 per cent., vegetable 12.1 per cent., hypophosphites.

Diet No. 10: Calories 2,670; nutritive ratio 1:5; fat to carbohydrate 1:1; pure vegetable diet, nut protein predominating: nuts 66.2 per cent., vegetable 17.7 per cent., cereal 14.8 per cent., fruits 1.3 per cent.

Diet No. 11: Calories 4,285; nutritive ratio 1:20; corn products diet with gelatin, being an amino-acid deficient diet.

Diet No. 12: Same as Diet 11 with casein added, making the diet an amino-acid sufficient diet.

Exact quantities used in Diets 9 and 10 are given.

One of the questions which by the use of these diets we sought to answer was this: Was there any difference in the quantity of milk protein produced when mothers were fed on a wide or a narrow nutritive ratio?

Tables 3-7 are submitted as an answer to this question:

TABLE 3.—Nitrogen Balance Sheet on Animal Protein Diet

Diet No.	Nutritive Ratio	Nitrogen, Grams in 24 Hr.						Name of Mother
		Intake	Feces	Absorbed	Urine	Milk	Balance	
9	1:4	20.64	1.63	19.01	9.54	2.63	+6.81	Ruth
9	1:4	20.64	1.60	19.04	9.79	2.23	+7.01	Grace
7	1:5	16.56	1.68	14.77	10.94	2.88	+1.04	Ruth
7	1:5	16.56	1.05	15.51	13.35	2.12	+0.034	Grace
1	1:6	19.60	1.83	17.76	9.45	2.88	+5.10	Ruth
1	1:6	19.60	1.53	18.06	10.92	2.35	+4.79	Grace
2	1:8	16.11	1.68	14.45	11.45	2.28	+0.71	Ruth
2	1:8	16.11	1.60	14.51	16.55	2.19	—4.24	Grace
6	1:6	14.68	1.66	13.01	12.70	2.39	—2.08	Ruth
6	1:6	14.68	0.98	13.69	14.12	1.68	—2.11	Grace
6	1:6	13.94	1.38	12.56	6.32	1.26	+4.72	Mary
6*	1:6	14.75	0.231	14.52	5.22	1.62	+7.66	Mary

* Diet same as No. 6 with the addition of 250 c.c. cow's milk.

It will be seen that when diets were given containing a narrow nutritive ratio the actual number of grams of nitrogen excreted in the milk was greater than when fed on a wider nutritive ratio. Not only was this true, but the mothers were in positive nitrogen balance on the narrow ratios, while on the wider ratios they went into negative balance and were forced to give up some nitrogen to keep up the milk production, thus "milking the flesh off of their backs." These facts hold

true only when the protein in the diet is from animal source. It is difficult to keep the mothers in positive nitrogen balance regardless of how narrow a ratio is fed when given vegetable protein, as is shown by Table 4.

TABLE 4.—Nitrogen Balance Sheet on Vegetable Protein Diet

Diet No.	Nutritive Ratio	Nitrogen, Grams in 24 Hr.						Name of Mother
		Intake	Feces	Absorbed	Urine	Milk	Balance	
10	1:5	16.75	1.68	15.07	12.99	2.79	—0.711	Ruth
10	1:5	16.75	1.67	15.08	16.77	2.50	—1.69	Grace
3	1:9	12.71	1.46	11.32	8.76	2.46	+0.093	Ruth
3	1:9	12.71	1.68	11.03	9.75	1.84	—0.559	Grace
8	1:13	6.09	1.77	4.32	8.77	2.45	—6.90	Ruth
8	1:13	6.09	2.15	3.94	7.32	2.04	—5.38	Grace

It will be noted that there is a marked difference, viz., the mothers were thrown into negative nitrogen balance even when fed on a narrow nutritive ratio when the protein supplied was of the vegetable type.

This leads us to the second question which these observations were designed to answer: What type of protein is best adapted to the production of milk protein? What has been shown in Table 4 is much more convincingly shown in Tables 5 and 6.

Table 5 shows that the mothers, when fed on diets predominating in animal protein, remain in positive nitrogen balance as long as the nutritive ratio is 1:6 or narrower, and that above that they go into negative balance.

Table 6 shows the inadequacy of diets in which there is vegetable protein alone or in which it predominates. In Diets 8 and 10 there was vegetable protein only, which resulted in negative nitrogen balance, while in Diet 3 the single animal protein milk added to a vegetable diet was able to establish nitrogen equilibrium.

In estimating the efficiency of a diet one should take into consideration not only the amount of nitrogen excreted in the milk, but also the amount of nitrogen added to or withdrawn from the tissues of the mother. These two factors when considered in relation to the nitrogen absorbed gives an efficiency index.

Tables 5 and 6 show the efficiency of the various diets when considered from this standpoint.

It will be noted that the diets are arranged according to nitrogen efficiency and vary from 49 per cent. positively efficient to 100 per cent negatively efficient. It will be noted that diets 1, 7 and 9 have a narrow nutritive ratio and are made up of two-thirds or more of

animal protein. These diets give the best protection to the tissues of the mother. It will also be noted that the diet containing 3,767 calories (overfeeding) did not give as good a result as the diet containing 2,928 calories (overfeeding is not necessary).

TABLE 5.—Nitrogen Distribution and Efficiency Table on Animal Protein Diet

Diet No.	Nutritive Ratio	Food Calories	Milk Produced, C.c.	Milk, Calories	Percentage of Nitrogen Intake Found In: Milk	Feces	Urine	Retained	Efficiency	Name of Mother
9	1:4	2,927	1,522	968	12.7	7.9	46.3	+33.0	49.6	Ruth
9	1:4	2,927	1,630	1,192	10.8	7.7	47.4	+33.0	48.5	Grace
7	1:5	2,842	1,486	962	17.3	10.9	66.0	+ 5.6	26.4	Ruth
7	1:5	2,842	1,751	967	12.8	6.3	80.4	+ 0.3	13.9	Grace
1	1:6	3,767	1,475	1,042	14.7	9.3	48,5	+27.0	43.0	Ruth
1	1:6	3,767	1,445	1,071	12	7.8	55.7	+24.0	38.8	Grace
6	1:6	2,774	1,329	1,000	16	11.3	85.6	—13.3	2.3	Ruth
6	1:6	2,774	1,521	1,269	11	6.7	96.2	—14.3	—3.0	Grace
6	1:6	2,388	523	.....	9.05	9.9	45.0	+32.1	47.6	Mary
6*	1:6	2,560	666	.....	11.03	0.09	35.4	+52.0	74.2	Mary
6†	1:6	2,411	813	.....	26.4	10.9	58.4	+4.3	34.3	Mary
2	1:8	3,446	1,425	835	14.2	10.3	71.0	+4.3	20.7	Ruth
2	1:8	3,446	1,375	698	13.6	10.0	102.0	—26.4	—1.4	Grace

* Diet same as No. 6 with the addition of 250 c.c. fresh cow's milk.
† Diet same as No. 6 with the addition of 50 gm. malted milk.

TABLE 6.—Nitrogen Distribution and Efficiency Table on Vegetable Protein Diet

Diet No.	Nutritive Ratio	Food, Calories	Milk Produced, C.c.	Milk, Calories	Percentage of Nitrogen Intake Found In: Milk	Feces	Urine	Retained	Efficiency	Name of Mother
10	1:5	2,670	1,758	1,096	16.6	10.0	90.0	—4.2	13.8	Ruth
10	1:5	2,670	1,620	1,372	14.9	10.0	90.0	—10.0	5.3	Grace
3	1:9	3,503	1,370	824	19.3	11.0	88.0	+0.22	22.0	Ruth
3	1:9	3,503	1,174	766	14.4	13.0	86.8	—4.38	11.0	Grace
8	1:13	2,286	1,507	786	40.2	29.0	143.0	—113.0	—102.8	Ruth
8	1:13	2,286	1,586	973	32.8	35.0	120.0	—87.0	—8.6	Grace
4	1:15	3,634	1,362	970	27.6	26.3	95.8	—49.9	—30.2	Ruth
4	1:15	3,634	1,416	1,059	22.1	18.3	102.0	—42.4	—2.2	Grace

In Diets 3, 4 and 10, in which vegetable protein exceeded the animal protein, the efficiency was much diminished, though still sparing the maternal tissues. Special consideration should be given to Diet 10,

since it was a purely vegetable diet, 60 per cent. of its protein being derived from nut foods. The tissues were amply protected, and a large quantity of milk was produced containing more nitrogen and more calories in twenty-four hours than any other diet used in this series.

Diet 6 was just able to maintain nitrogen equilibrium, although nitrogen excreted in the milk was considerably lessened.

A diet which would just maintain nitrogen equilibrium is in many respects preferable to one which tends to add weight, many mothers complaining of this increase in weight during the nursing period. Diets 4, 5 and 8 put the mothers in negative balance. It will be noted that the ratios were wide, and in Diets 5 and 8 the calories were very low. These two diets were constructed so as to approximate diet lists secured from a number of mothers whose milk supply was failing. It is evident why a mother receiving only from 6 to 8 gm. of nitrogen a day cannot continue to give up from her own tissues an equal quantity of nitrogen, although nature will go to extremes in maintaining a milk supply.

The results obtained from a pure vegetable diet (Diet 8) suggest the futility of excluding from the diet at least a certain amount of animal protein. Many mothers are trained during the latter part of pregnancy to eliminate albuminous food from their dietary because of albuminuria. The fear that the albuminuria may persist during the puerperium causes many mothers to continued a low protein diet, which frequently is the cause of failing milk supply.

The question as to what form of animal protein is best adapted to the production of milk protein is an important one. There is considerable evidence that cow's milk protein, while not an essential part of a diet, contributes considerably more than its mere caloric value in increasing not only the protein output in the milk, but also aids greatly in protection of the maternal tissues from destruction. This is shown in results obtained in Diet 3, which was made up entirely of vegetable protein with the exception of milk which consisted of 23.5 per cent. of the protein fed. This small amount of animal protein was sufficient to keep the mother in positive nitrogen balance and produce more calories (1,590), and more milk nitrogen (2.46 gm.) in the milk produced than Diet 2, which contained 50 per cent. animal protein, a small proportion of which was derived from milk. Hart and Humphrey found that milk protein when fed to cows had an efficiency for milk production and tissue preservation of about 60 per cent. in dairy cows, while corn and wheat protein had an efficiency of 40 per cent. and 36 per cent., respectively.

The effect of milk protein on tissue preservation as well as its effect on milk nitrogen is shown in Table 7.

TABLE 7.—Effect of Milk Protein on Tissue Preservation and Milk Nitrogen

Diet No.	Nitrogen Absorbed Four Day Period	Nitrogen in Milk	Nitrogen in Milk of Tissue Formed or Destroyed	Nitrogen Efficiency
6	50.242	5.04	23.949	47.60
6*	58.082	6.48	37.176	74.2

* 250 c.c. of fresh cow's milk added to Diet 6.

From Table 7 it will be seen that by the addition of 8 ounces of milk daily to a diet previously poor in milk protein the efficiency of such diet was raised from 47.6 per cent. to 74.2 per cent., and that the nitrogen of the milk was raised from 5.04 gm. to 6.48 gm.

SUMMARY

1. A nutritive ratio of 1:6 or narrower seems best adapted to the need of nursing mothers. (This ratio refers to the proportion of digestible protein to digestible fat and carbohydrate, the latter reduced to a carbohydrate basis.)

2. Animal protein is more suitable than vegetable protein in supplying nitrogen for milk and maintenance of nitrogen balance.

3. The protein derived from nuts when fed with other vegetable protein is suitable for supplying milk protein and for maintaining nitrogen equilibrium.

4. A diet composed exclusively of cereals, fruits and vegetables does not supply sufficient protein for elaborating milk protein and causes a severe drain on tissues of mother.

5. Of the various forms of animal protein, that which is derived from cow's milk, seems particularly suitable for the production of human milk protein, as well as for the preservation of maternal tissues.

CONGENITAL SKIN DEFECTS *

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CHICAGO

The so-called congenital skin defects have not been recorded frequently in the literature. The majority of the accessible reports deal with skin defects of the scalp, which vary in size from a pinpoint to a small coin. They are usually circular in shape, sometimes oval or irregular, and generally have clean-cut edges.

The first authentic case seems to have been recorded by an English physician, Campbell, who in 1826 reported a skin defect of the scalp the size of a crown, which assumed the characteristics of a progressive ulcer. Priestley, in 1859, reported a congenital skin defect over the anterior fontanel about the size of a shilling. The defect healed in a short time, the process of repair beginning at the edge of the ulceration. Billard, in 1828, reported a case of skin defect over the parietal bone supposed to have been caused by a uterine polyp of the mother. Emanuel, in 1905, reported an infant with congenital absence of skin involving hands, legs and feet. The child was born dead. There was no evidence of syphilis. Numerous reports have been published from time to time which will be referred to in tabulated form and in the references at the end of the article.

Most writers on the subject of congenital defects attribute them either to errors in development, or to inflammatory adhesions between the external layers of the skin and the amnion. At the point where this adhesion has taken place, the growth of flat epithelium is retarded. As the liquor amnii accumulates, the so-called Simonart's bands are formed. These are adhesions which form threads or bands between the amnion and the fetus. If these bands are torn loose from the integument of the fetus, a skin defect remains. Not infrequently, these skin defects are associated with other congenital malformations, for instance, with deformities of the extremities such as deficient fingers, hands, or feet.

As has already been noted, the lesions are found most frequently on the scalp. They may occur, however, on the trunk, though in one case reported by Bürger, in addition to the scalp defect, ulcerating lesions occurred on both knees and on both elbows. Macé reported an infant who at the time of birth showed these characteristic defects

* Read at the meeting of the American Pediatric Society, White Sulphur Springs, W. Va., May 28, 1917.

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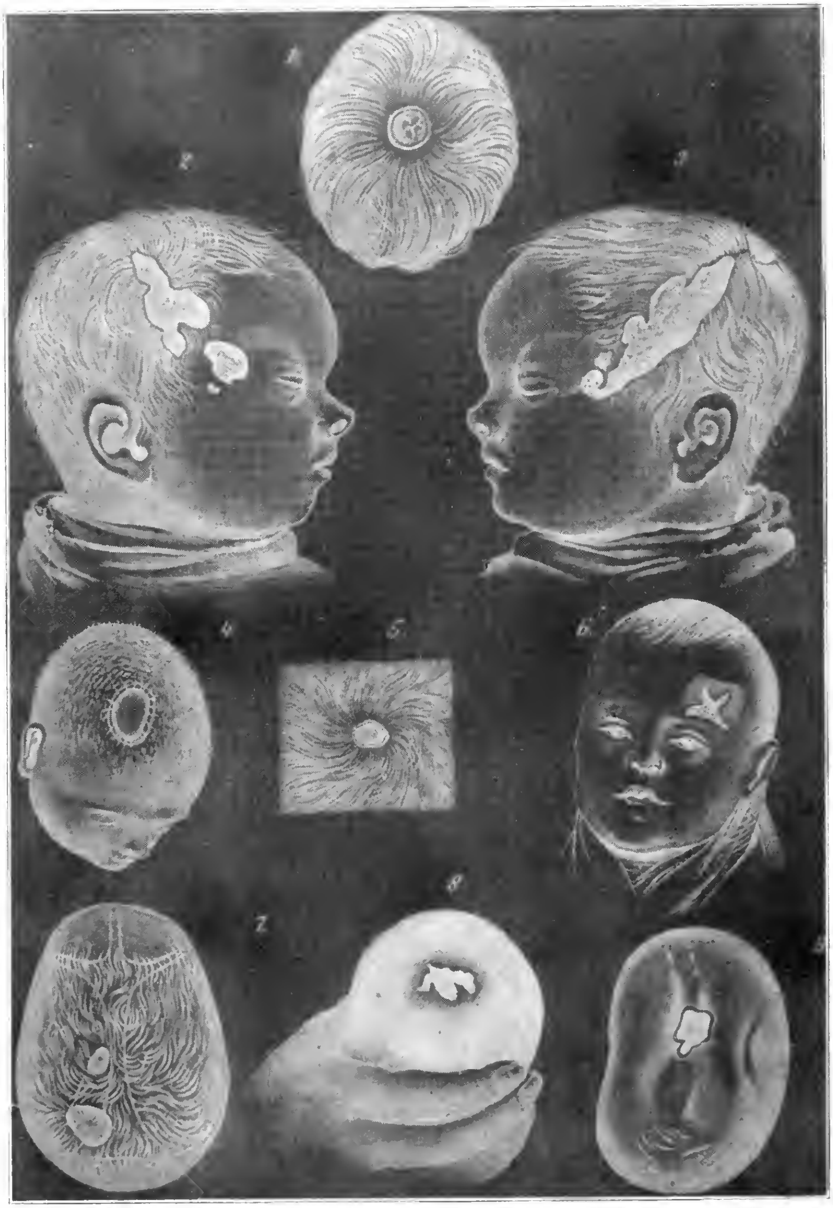

Fig. 1.—Reported cases of skin defect of the scalp. 1, Priestley's case; 2 and 3, von Hebra's case; 4 and 5, von Hofmann's; 6, Dohrn's; 7, Bonnaire's (3d), 8, Bonnaire's (4th); 9. Mathe's (1st). See accompanying table.

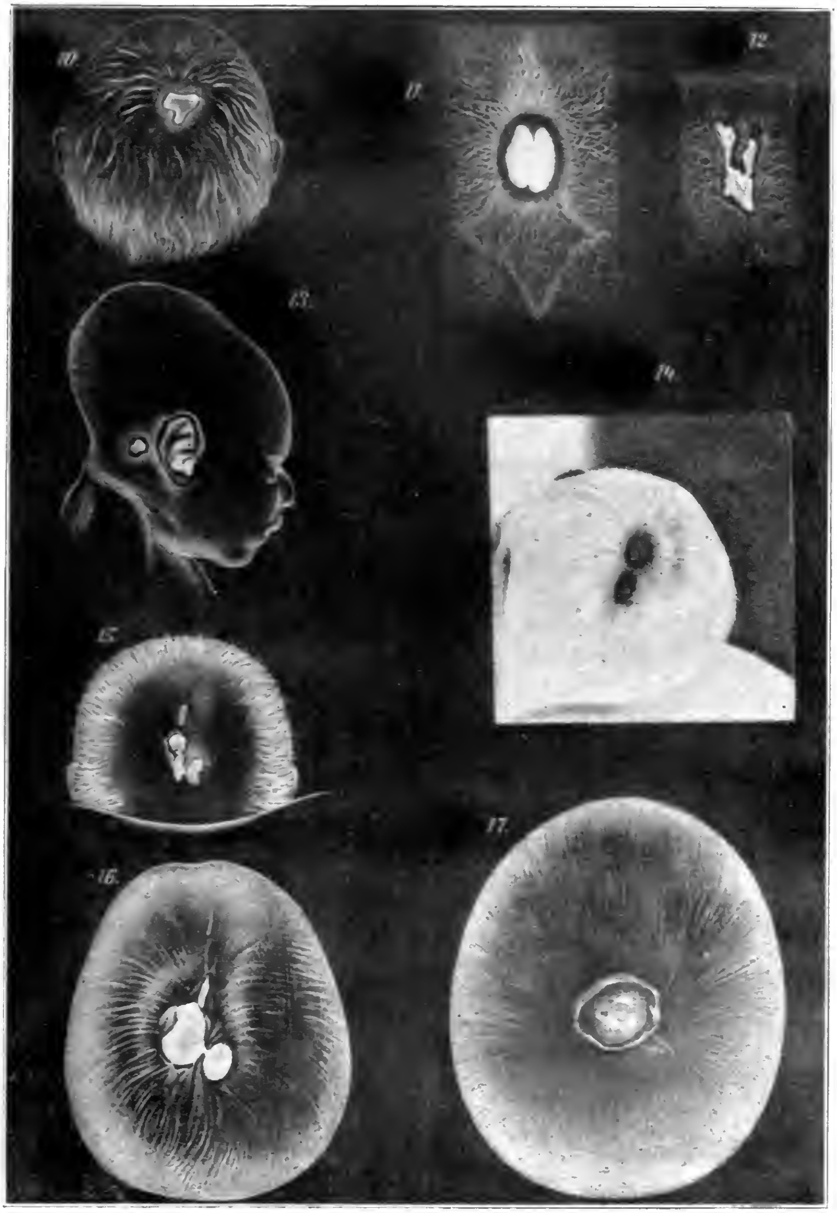

Fig. 2.—10, Mathe's (2d) case; 11, Dittrich's (1st); 12, Dittrich's (2d); 13, Schultze's; 14, von H. Vörner's; 15 and 16, Winckel's; 17, Keller's case. See accompanying table.

on the right buttock. This lesion was about 3 cm. in circumference, bled readily, and had a red periphery. The same author reported another infant with a congenital, ulcerating skin defect on the right forearm and a cicatrized defect on the left. The ulcer healed promptly. Emanuel's report, previously mentioned, refers to congenital skin defects occurring on hands, legs, feet, over the temples and the bridge of the nose, and also an area in the middle of the lumbar region.

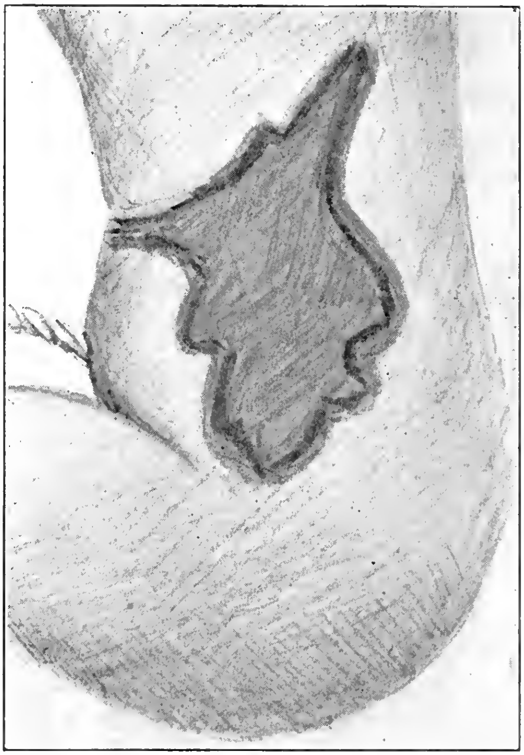

Fig. 3.—Hahn's case showing one side of a bilateral skin defect on lateral portion of the trunk.

The defects are usually visible at birth. They seem to bear no relation to trauma during parturition, and undoubtedly originate *in utero*. Occurring singly or in groups, they present ulcerated areas which affect both layers of the skin. The subcutaneous tissues are not involved. The ulcerated areas, as in my case, are sharply defined, somewhat irregular in outline; the base of the ulcer is red and secretes a thin lymph.

Of the histologic examinations made in these cases, Keller found that minute hairs occurred in the affected area. It should be remarked,

however, that this finding is contrary to other histologic reports. In some of the recorded cases, the area involved developed hairs later in life. Microscopic examination not only shows the failure of the epidermis to develop, but also, that the skin glands, if they develop at all, do so in a rudimentary manner. It is worthy of note that the microscopic examinations fail to show any old or recent degeneration in the disease area or in the surrounding tissue. This would tend to exclude a secondary process due to some intra-uterine inflammation. It is noteworthy that microscopically the area under examination shows the absence of epithelial structures, smooth muscle and adipose tissue.

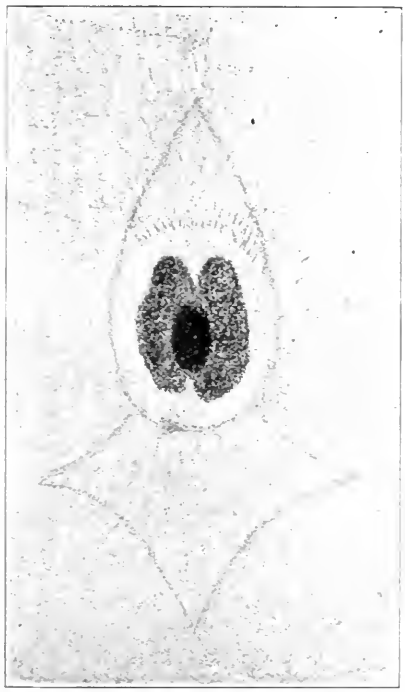

Fig. 4.—Dittrich's case of skin defect of the scalp.

Because of the well developed connective tissue, one is led to assume that this defect of skin can be traced to the early period of embryonal life. Because the lesions occur early in fetal life, the hair buds do not develop and the sebaceous glands fail to appear or are rudimentary. That the defects are not due to an injury is shown by the fact that they are already present in early fetal life. The condition has been referred to as a congenital atrophy of the skin, but this can hardly apply for the reason already mentioned, namely, that atrophy implies degeneration, and no degenerative process can be demonstrated. There is an abundance of connective tissue present in

Congenital Skin Defects of the New-Born

Reporter and References	Sex and Age	Localization and Character of Defect	Remarks
Campbell: Edinburgh Jour. Med. Sc., 1826, **5,** 82.	New-born	Parietal; circular defect, 3¾ cm. in diameter; ulcer with progressive characteristics	....
Same as above	New-born	Parietal; scarry ulcer	....
Billard: Traité d. mal. d. enf., New Series, Paris, 1828, p. 232.	New-born	Left parietal; about 1½ in. by ⅓ in. defect	There was a polyp involving uterus of mother, which caused destruction of part of uterine wall.
Abele: Med. Cor.-Bl. d. Wurten. ärzt. Verein, 1835, **5,** 1.	New-born	Upper half of left frontal region; 1½ by 1 inch wide; skin defect	Trauma; mother injured 10 weeks before.
Dieterich: Würtemb. Kor.-Bl., 1838, p. 5.	New-born	Round defect, 1¼ cm. in diameter; granulated; scar 1 by 1½ inches; frontal region	Trauma; mother injured 10 days before birth.
Hahn: Jour. d. Chir. u. Augenh., 1840, **30,** 156.	New-born	Large irregular defects on right and left side of trunk; almost symmetrical; defects united above navel	....
Priestley: Trans. Obst. Soc. London, 1859, **1,** 60.	New-born	Circular defect, 2¼ cm. in diameter, of small fontanel; healing beginning at edge	....
Schatz: Monatsschr. f. Geburtsh., 1869, **34,** 110.	10 days old	Right side of head; 7½ cm. long; skin erosion	Pelvic exostosis; possibly the erosion was due to injury by finger nail of nurse.
Tarnier: Union méd., 1872, **33,** p. 391.	1 day old	Parietal; covered by fine scar	....
v. Hebra: Mitteil. d. Wien. embryol. Inst,. 1882, **2,** 85.	Full term	Both sides of head, 6 cm. by 4 cm. and 12 mm. by 5 cm., respectively; long, thin strips of defect; serous fluid beneath	Definite development of connective tissue.
v. Hofmann: Wien. med. Presse, 1885, No. 18; also Lehrb. d. gericht. Med., 1895, Part 2, p. 776.	4 mos. fetus	Large fontanel; 1 cm. size; granulated defect	Author considers these cases due to Amniotic adhesions (Amniotische Bände).
Same as above	Female, full term	Parietal; 5 to 6 cm.; glossy appearing defect	
Same as above	Male, full term	Parietal; circular defect; 4 cm. in diameter	
Dohrn: Ztschr. f. Geburtsh. u. Gynäk., 1888, **14,** 366.	New-born	Left frontal region; crusted strip, 1 cm. long; red granulation; excorciated	....
Bonnaire: Progès méd., 1891, **13,** 481 and 497.	Two full-term children	Sagittal suture; defect 3 cm. in diameter; gelatinous surface	Microscopically examined; thinks due to amniotic bands or adhesions.
Same as above	7½ mos. fetus	Small fontanel circular defect, 1¼ in. in diameter size; pale covered defect; 2 smaller defects; one in sagittal suture; one in occipital region	Microscopically examined; deformed in several ways; hydrocephalus, hydramnion, etc.; amniotic bands, author thinks cause.
Same as above	One of full-term twins	Middle of sagittal suture; 12 mm. diameter; gelatinous surface	Amniotic bands author thinks cause.
Same as above	Full term child	L. os parietal; midline small bean-sized ulcer; scar tissue (hydramnion case)	Microscopically examined; same cause as above
Schrader: Zentralbl. f. Gynäk., 1893, **17,** 374.	Full term	7 cm. by 1 cm. left of parietal; blood crust	Hydrocephalus externus; died 3 months later.
Mathes: Inaugural Diss. Marburg, 1894.	25 cm. long fetus	Parietal; 6 by 8 cm. size defect with glazed surface	Microscopically examined; author thinks cause is amniotic adhesions.
Same as above	Full term child	2 cm. in front of small fontanel; irregular triangular; granulated surface	

CONGENITAL SKIN DEFECTS OF THE NEW-BORN—(*Continued*)

Reporter and References	Sex and Age	Localization and Character of Defect	Remarks
Dittrich: Vierteljahr. f. gericht. Med., 1895, **9**, 258.	New-born	Parietal; 20 by 17 sq. mm.; blackish skin defect	Histologically examined.
Same as above	?	Middle of sagittal suture 2.5 by 1.5 cm. defect; 2 smaller defects over the small fontanels	
Schultze: Ztschr. f. Geburtsh. u. Gynäk., 1895, **31**, 225.	Full term	Left frontal bone, irregular spur with skin injury; similar behind external ear, 1 cm. size.	Bone injury due to passage of head in the promontory; defect due to amniotic band.
Volkmann: Berl. klin. Wchnschr., 1898, **35**, 1025.	Full term	L. parietal; part of small fontanel; 2 bean-sized defects; granulated	Author thinks cause is amniotic adhesions.
Weindler: Zentralbl. f. Gynäk., 1899, **23**, 414.	3 weeks old child	Small fontanel; circular defect, 1¾ cm. in diam.; hard defect with granulated surface; flat edges	Author thinks cause is amniotic adhesions.
Alain: Jour. méd. de Bordeaux, 1901, **31**, 388.	Full term	2 cm. in font of large fontanel 7 sq. cm. size defect; smaller defect to the left	....
Macé: Bull. Soc. d'obstétrique, Paris, 1901, **4**, 8.	New-born	Circular defect 3 cm. in diam. on buttock; sphacelic plaque surrounded by inflammation	....
Same as above	New-born	Ulceration 3 cm. by 5 cm. on right forearm; same, but cicatrized on left forearm	....
Vörner: Arch. f. Dermat. u. Syph., 1903, **66**, Part 3, p. 407.	4 year old boy	Defects on right and left side of parietal, one about 25 sq. mm., the other 15 mm. in size	Histologically examined aplasia.
Bürger: Zentralbl. f. Gynäk., 1903, **27**, 644.	Full term (13 days old child)	Parietal, rayed scarry defect; defects also on both knees and both elbows (excoriation or ulceration)	Author thinks amniotic adhesion developed from an abdominal injury received by mother in 4th month of pregnancy.
Müller: München. med. Wchnschr., 1903, **68**, 1065.	Female, 32 yrs.; defect since birth	Pronounced erythema pudoris on chest, neck and face; spots size of quarter	Due to faulty development of skin, causing innervation of blood vessels.
Same as above	Male, 48 yrs.; defect since birth	Defect similar to above	Due to same cause as above.
Winckel: Samml. klin. Vortr., 1904, Nos. 373 and 374.	Full term	Small fontanel; suppurative defect	Harelip, cleft-palate, etc.
Emanuel: Report Soc. for Study Dis. of Child., 1905-1906, **6**, 157.	Stillborn at full term	Absence of skin on hands, legs, feet, over temples, nose, middle lumbar region	Arrest of development of layers of epidermis.
Keller: Vierteljahresschr. f. gericht. Med., 1908, **35**, 223.	6 mos. fetus; 25 cm. long	Defect on right side of head; skin bluish-red; 1 sq. cm. size defect; mainly in parietal region in sagittal suture	Fetus extracted manually after dilatation; uterine hemorrhage; author thinks defects due to amniotic adhesions.
Liedig: Ztschr. f. Med.-Beamte, 1908, **21**, 607.	Full term	Circular defect 6 mm. in diam. on head	Occurred in utero.
Schulte: Deutsch. med. Wchnschr., 1909, **35**, 86.	24 hour old	On left parietal bone and sagittal suture above small fontanel; 6 by 5 cm.	....

these lesions, and consequently the defect resembles hypertrophy more than atrophy.

If one investigates the recorded cases, it is found that these defects have been observed both in stillborn children and those who died shortly after birth, as well as in normal children who survive. Unless the skin defect is wide in extent, there is no apparent reason why the slight malformation should of itself be incompatible with the life or the general health of the infant. The local skin condition is sufficient to explain the failure of hair follicles and sebaceous glands to develop. The majority of lesions tend to cicatrize in a short time, thus providing an adequate covering for the denuded surface.

From the standpoint of differential diagnosis, it may be thought that possibly these lesions are due to trauma. We have already pointed out that there is no inflammatory reaction and no degenerative process in the region of the defects. In the case which came under my observation, the lesions were round and symmetrical, and, as in most of the reported cases, the birth was normal.

REPORT OF CASE

The case which has led to this brief clinical report was a newly born infant that was referred to me by Dr. J. B. DeLee of the Chicago Lying-In Dispensary. The mother had previously borne four perfectly normal children. Both parents were in good health. The labor was normal and the baby was normal in weight and size. It presented a defective skin area over each knee. These areas are well shown in the accompanying colored drawing (Fig. 1). They were about 1 by 1¼ inches in area; they were symmetrical, that is, almost identical in size and shape; they seemed to be, so to speak, irregularly punched out. The skin around the edges was drawn and puckered, presenting the appearance of ulcers with irregular edges. The base was beefy red and moist. A few small foci on this red, ulcerated surface showed a yellow exudate. A whitish scar seemed to cross the ulcerated area, appearing like a connective tissue band, which indicated the beginning of cicatrization. It may be said that from week to week the ulcers gradually covered over, so that after five or six weeks the denuded, red areas were replaced by shiny, white patches, somewhat lighter in color than the surrounding skin. The healing process was complete, and the baby appeared normal in every respect.

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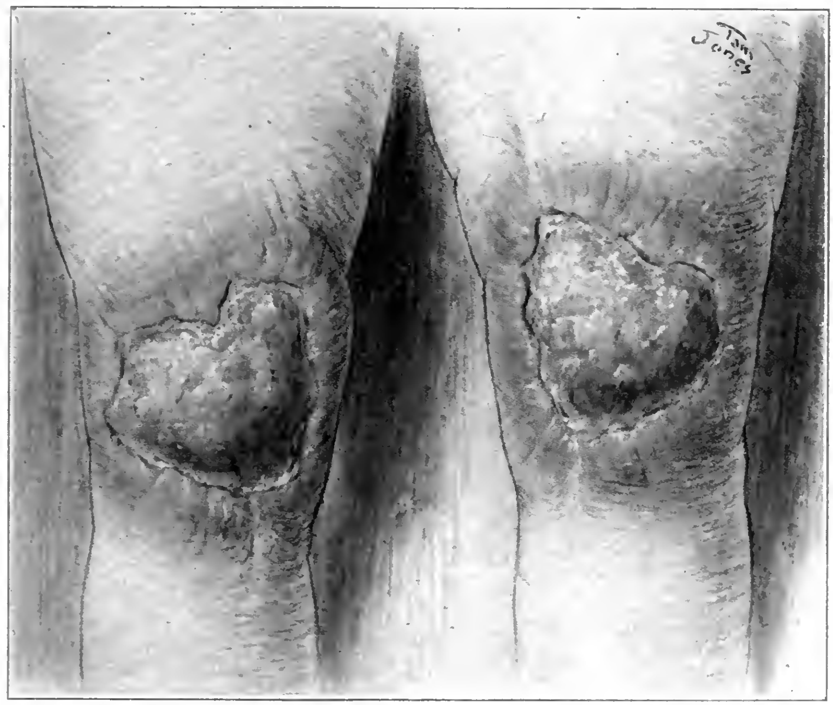

Fig. 5.—Author's case of bilateral skin defect of the knees.

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Liedig: Zur Kenntnis der kongenitalen Hautdefekte am Kopf der Neugeborenen, Ztschr. f. Med. Beamte., Berl., 1908, **21,** 607.

Keller: Zur Kenntnis der kongenitalen Hautdefekte am Kopf d. Neugeborenen, Vierteljahrss. f. gericht. Med., 1908, **35,** 223.

Schulte: Demonstrationen eines Neugeborenen mit Hautdefekten am Schadel, Deutsch. med. Wchnschr., 1909, p. 86.

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Macé: Exulceration d'origine congenitale chez deux nouveau-nés, bien pratants à type spacelique chez l'un d'eux, Bull. Soc. d'obst. de Par., 1901, **4,** 8.

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Tott: Eigentümliche Arten von Hautleiden bei Neugeborenen, Ztschr. f. Geburtsh., Berlin, 1841, **10,** 25.

PROGRESS IN PEDIATRICS

REVIEW OF POLIOMYELITIS *

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HISTORICAL

In the middle of June, 1916, announcement was made of a group of cases of infantile paralysis in Brooklyn, New York.[1] During the summer the disease assumed the proportions of a great epidemic which, in its severity and extent of territory involved, is probably unprecedented. There were 24,000 cases in the United States.[2] About one-half of these were reported in the state of New York. In New Jersey, Connecticut, Massachusetts, Minnesota, Delaware, Rhode Island and Pennsylvania, the epidemic was also extensive. In four states, no cases were reported. These were Nevada, New Mexico, Georgia and California.[3]

EPIDEMIOLOGY

The epidemiologic characteristics of this disease have been the subject of numerous reports, the sum of which not only conflict with the conception of the disease presented from an experimental aspect, but do not harmonize with generally accepted ideas regarding other infectious diseases.

Various observers have differed regarding its mode of transmission, some favoring the human contact theory, others favoring the "place infection" theory, thereby incriminating the food supply, domestic animals, insects or other local environmental factors in the transmission of poliomyelitis.

Frost[4] summarizes these data. Epidemics offer unexplainable irregularities in their geographic distribution. While most available data suggest that the disease distributes itself from place to place along avenues of public travel, there are notable exceptions. The epidemic which occurred in New York City in 1907 did not extend to Phila-

* Submitted for publication July 1, 1917.

1. Medical News: Jour. Am. Med. Assn., 1916, **66,** 2076.
2. Emerson, Haven: Bull. Johns Hopkins Hosp., 1917, **28,** 131.
3. Lovett, R. W.: Jour. Am. Med. Assn., 1917, **68,** 411.
4. Frost, Wade H.: U. S. Public Health Service, Hyg. Lab. Bull. 90; U. S. Public Health Reports, Reprint 350.

delphia despite its close communication. In 1910, a severe epidemic occurred in Washington, D. C., and a smaller outbreak in Philadelphia, while Baltimore, lying between these two cities, escaped with only a few cases. Such instances lend support to the theory of infection by other factors than the human carrier, such as an infection of local water or food supply, or one carried by insects or domestic animals. On the other hand, the rapid extension of the disease along foci radiating from the original source of infection is in favor of the "human traffic" idea, rather than that of "place infection." This irregularity of distribution finds an analogy in the transmission of cerebrospinal meningitis, a disease which appears to be directly contagious. The maximum prevalence of the disease in the summer is a rather constant characteristic which has been used as an argument against its being carried by contact infection, since in this respect it is unlike the other contagious diseases, so carried, whose maximum prevalence is in the winter months. On the other hand, Frost states that "cases have occurred during the last few years in every month of the year." This constant presence of the disease disproves the hypothesis that a new epidemic may be ascribed to the introduction of a new infection.

The small total incidence of the disease has been a puzzling feature in its study. It has been further observed that in such an affected locality, the epidemic will not likely recur for at least two years.

In rural communities the incidence of the disease has been greater than in thickly settled centers, which occurrence is quite in contrast to such diseases as measles and scarlet fever.

Hygienic conditions, which generally bear a relationship to the incidence of an infectious disease, do not seem to play a very important rôle in the occurrence of poliomyelitis, as cases have occurred in the best hygienic surroundings.

The most striking constant about the occurrence of the disease has been its great frequency in very young children, among whom the disease is fifty times more prevalent than among young adults. This greater incidence among young children has been used as an argument favoring various modes of infection. That children use milk more generally than adults, that they wear scantier clothing, that they are less cleanly, that they are more frequently in contact with street dust, have all been used to lend support to the respective theories incriminating the milk supply, insects, lack of hygienic surroundings, or street dust as factors in the spread of poliomyelitis. None of these hypotheses is supported by epidemiologic evidence. Neither is this enormous difference explained on the basis of a greater exposure, for by analogy with other communicable diseases, such an argument cannot be supported. It can only be assumed that children are more susceptible.

The paralytic diseases which are said to occur among domestic animals simultaneously with epidemics of poliomyelitis, have neither proved to be examples of poliomyelitis, nor have they been noted in greater frequency during the prevalence of an epidemic.

While weather conditions have been suggested as supporting the hypothesis of a deficient rainfall having a direct bearing on the cause of an epidemic, experience has not confirmed the point of view. An epidemic may be declining and developing in closely approximated communities under similar meteorologic conditions.

The evidence regarding the contagiousness of the disease is very conflicting, as only a small percentage of patients give a history of contact with other infected persons. To explain the discrepancies between known contacts and instances of the disease, the existence of healthy carriers must be assumed. That such carriers exist has been proved experimentally by Flexner[5] and others.[6] The difficulties of artificially cultivating the organism which produces the disease makes impossible the routine recognition of such carriers. Recovered patients may also constitute carriers of the infectious agent.[7]

A third group, the one which in the opinion of all observers plays the most important part in the unexplainable transmission of the disease, is the group of so-called "abortive" cases, many of which pass undiagnosed. Irrespective of the type of the disease, the infectious agent, or virus is present on the mucous membranes of the nose and throat and intestines.[8] These parts of the body not only act as points of exit for the virus, but it has been shown by Flexner and his co-workers that the infection atrium is by the nose and throat. Multiplying there, the virus is readily distributed "by coughing, sneezing, kissing and by means of fingers and articles contaminated with these secretions." The virus is, moreover, resistant to high temperature and drying, so that when it is thrown off from the body, the dried secretions may, in the form of dust, constitute a potential source of infection. Regarding the conveyance of the disease by insects, "neither mosquitoes nor lice seem able to take the virus from the blood of infected monkeys." The domestic fly may conceivably act as a mechanical carrier by coming in contact with infective secretions. Flexner considers reported simultaneous instances of paralysis among domestic animals as pure coincidences, since all such instances have never proved, on proper examination, to be poliomyelitis.[9]

5. Flexner, S.: Jour. Am. Med. Assn., 1916, **67,** 279.

6. Lucas, W. P., and Osgood, R. B.: Jour. Am. Med. Assn., 1913, **60,** 611; quoted in Jour. Am. Med. Assn., 1916, **67,** 118.

7. Flexner, S.: Am. Jour. Dis. Child., 1915, **9,** 353.

8. Sawyer, W. A.: Am. Jour. Trop. Dis. and Prev. Med., 1915, **3,** 164. See also Footnote 5.

9. Flexner, S., and Clark, P. F.: Jour. Exper. Med., 1913, **17,** 577.

The fluctuations in the severity of an epidemic, Flexner[10] explains as analogous with the fluctuation in the infectiousness of the microorganism on passage through several generations of animals, plus the variation in individual susceptibility.

Lavinder[11] notes that all epidemiologic studies relative to the disease have been directed toward either proving or disproving Wickman's hypothesis that poliomyelitis is a contact disease. While receiving the qualified approval of both epidemiologic and experimental studies, several inconsistencies make further research necessary. These inconsistencies and the fact that healthy carriers and "missed" cases constitute the greatest source of transmitting the disease, make the control of the disease very difficult.

Fronczak[12] concludes that "there must be other sources of infection than those now known." Of the cases studied in Buffalo in 1912, only 18 per cent. of the patients gave any history of contact with a previously known case. Dividing the city wards into two groups, one-half containing those with the smallest population, "it was found that where the proportion of cases was the lowest, the average density was twice as great."

Emerson[13] notes a similar occurrence in regard to the comparative prevalence in various parts of greater New York. In the Boroughs of Queens and Richmond, where the congestion was least, there were more cases in proportion to the population. Other experiences, however, emphasize the rôle played by the human carrier. The experience of the children isolated in the institutions of New York City is particularly noteworthy. In these institutions, housing a total of about 28,000 children, quarantine against visitors and new admissions was ordered when the epidemic began. Only two cases of poliomyelitis developed, "one child developing the disease on August 8, simultaneously with the child of the engineer of the institution who lived outside the grounds, his house, however, abutting the buildings of the institution, and who had been in the habit of bringing in his child in its carriage each day and keeping it in the garden near the power house." The other case was not absolutely characteristic of poliomyelitis.

An experience which bears out the assumption that hygienic conditions play no rôle is related by Emerson:

Barren Island, situated in Jamaica Bay, is a place to which all the city garbage is brought by boat. All the city's dead animals, often two or three thousand a day, are brought here; it has no public water supply, no sewerage system, the

10. Flexner, S.; Clark, P. F., and Amoss, H. L.: Jour. Exper. Med., 1914, **19,** 195.
11. Lavinder, C. H.: Arch. Pediat., 1916, **33,** 847.
12. Fronczak, Francis E.: New York State Jour. Med., 1916, **16,** 389.
13. Emerson, Haven: Bull. Johns Hopkins Hosp., 1917, **28,** 131.

houses have no cellars, no garbage collection, and the people have few garbage cans, the household waste being thrown on the ground about the shanties. There are 17,000 people on the island, 350 of them being children, but there was no case of poliomyelitis on that island all summer. Smells, flies and insanitary conditions have prevailed, but because of its geographical position and the social condition of its people, the island is more or less isolated.

Craster,[14] reviewing the experiences of Newark in the recent epidemic, concludes that poliomyelitis is carried from place to place by human carriers. On no other basis can the spread of the disease in Newark be explained. A few instances of paralysis in lower animals which occurred during the epidemic proved not to be poliomyelitis. The occurrence of 83.8 per cent. of the cases in children under 5 years of age, and the apparent fluctuation of incidence with weather conditions, were the only outstanding features of the epidemic.

Kerley[15] studied the possibilities of contact in the spread of the disease. The instances selected were from an isolated community near his home. In all the cases detailed Kerley determined either transmission by an infected person or by an innocent carrier.

Sheppard[16] suggests that the term "contact infection" as used in regard to poliomyelitis must include instances of direct or indirect contact. The latter he refers to as the "social contact" factor. By such inclusion, any object which had previously been in intimate touch with an infected person would constitute a source of infection.

Murphy's[17] experience with poliomyelitis in the Crow Reservation upholds the contact theory. The persons affected all belonged to a group that had visited an infected district. No other individuals but those accounted for in this way developed the disease.

Richardson[18] is still of the opinion that insects may play a part in the transmission of the disease. According to his theory, rats are previously infected, the disease then being transferred to man by the agency of the flea.

Bodine[19] discusses the possible etiologic relationship of certain insects to the spread of poliomyelitis. The biennial occurrence of the disease suggests the tick as a possible carrier; the mosquito comes under suspicion by the seasonal prevalence of the disease. He refers to Rosenau's early work on the stable-fly, which in geographic distribution, its abundance under rural as well as urban conditions, correlates the incidence of poliomyelitis.

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14. Craster, C. V.: Jour. Am. Med. Assn., 1917, **68**, 1535.
15. Kerley, C. G.: Arch. Pediat., 1917, **34**, 32.
16. Sheppard, P.: New York State Jour. Med., 1916, **16**, 442.
17. Murphy, J. A.: Jour. Am. Med. Assn., 1916, **67**, 1247.
18. Richardson, M. W.: Boston Med. and Surg. Jour., 1916, **175**, 397.
19. Bodine, J. H.: Jour. Am. Med. Assn., 1916, **67**, 1872.

Dingman[20] records the occurrence of an epidemic possibly milk-borne. In three widely separated boarding houses, Dingman found several instances of poliomyelitis. All of these patients had used the milk from a particular dairy. This same dairy supplied three other houses, in which no cases occurred. On investigation, Dingman found that the residents of the last three always boiled their milk, while those of the first three used the milk raw. At the home of the dairyman there had been a case of illness in a 4-year-old boy which had been undiagnosed. The boy showed a beginning paralysis of his right leg. In the same frame dwelling, another child had been acutely ill, and at the time of observation was walking about, "dragging one foot as he walked." The cases mentioned were the only ones which had developed up to that time and for some weeks later in this locality.

The committee of the American Public Health Association concludes from a study of the disease that infection may be directly spread from person to person. They believe that the apparent inconsistencies which occur in tracing individual cases are explained by the lack of means for detecting mild cases, and by the possibility that such cases and healthy carriers are more numerous than frankly paralyzed cases. It is said:

> Many facts, such as the seasonal incidence and rural prevalence of the disease, have seemed to indicate that some insect or animal host, as yet unrecognized, may be a necessary factor in the spread of poliomyelitis, but specific evidence to this effect is lacking, and the weight of present opinion inclines to the view that poliomyelitis is exclusively a human disease and is spread by personal contact, whatever other causes may be found to contribute to its spread. In personal contact we mean to include all the usual opportunities, direct or indirect, immediate or intermediate, for the transference of body discharges from person to person, having in mind as a possibility that the infection may occur through contaminated food.

BACTERIOLOGY

In 1913, Flexner and Noguchi[21] reported the successful cultivation of a minute, filtrable micro-organism from cases of poliomyelitis. This was accomplished by inoculating tall tubes of human ascitic fluid containing sterile rabbit tissue, under anaerobic conditions, with pieces of nervous tissue obtained from poliomyelitic sources. These micro-organisms were described as minute, "globoid bodies measuring from 0.15 to 0.3 micron in diameter, and arranged in pairs, chains and masses, according to the conditions of growth and multiplication." No gas or acid was produced when various sugars and alcohols were added. The micro-organism behaved in a variable way toward the gram stain. Among its other properties were resistance to freezing,

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20. Dingman, J. C.: New York State Jour. Med., 1916, **16,** 589.
21. Flexner, S., and Noguchi, H.: Jour. Exper. Med., 1913, **18,** 461.

phenolization and glycerolation.[22] Growth occurred slowly, and was best demonstrated about the sixth or seventh day. With these cultures, poliomyelitis was reproduced and the organisms again recovered from the infected animals — thus fulfilling Koch's classical requirements.

In succeeding publications on the etiologic relationship of this micro-organism to poliomyelitis, Flexner and his associates reported the cultivation of the same micro-organism from the blood of infected monkeys[23] and otherwise added much to our knowledge of the pathogenesis of this disease.[24]

It was therefore with much surprise to the students of this disease that reports were published by several independent investigators, recording the isolation of a peculiar polymorphous streptococcuslike organism from numerous cases of epidemic poliomyelitis. This organism was isolated from the tissues of the central nervous system in nine of ten cases studied by Mathers.[25] In five instances the organism was obtained after death from the cerebrospinal fluid, and in one of two cases examined, in the mesenteric lymph nodes and kidneys.

Rosenow[26] has not only cultivated the organism from the brain and cord in every instance of twelve cases of poliomyelitis, but obtained the identical organism from the tonsils in a large series of patients with this disease.

Nuzum,[27] working independently of these investigators, contributes similar results. Later, Nuzum[28] also reported successful growth of the identical organism from the cerebrospinal fluid in forty of fifty fluids examined.

All of these investigators were, moreover, successful in reproducing the disease by injection of their cultures into rabbits and monkeys. Rosenow and his co-workers report successful results with guinea-pigs, cats and dogs; Nuzum and Herzog with lambs, all of which animals have heretofore been regarded as insusceptible to the disease.

The micro-organism obtained by these various investigators resembles in several respects the globoid bodies described by Flexner and Noguchi. Thus, it is resistant to glycerolation, passes through a Berkefeld filter and is neurotropic. Morphologically, a tendency to extreme irregularities was noted.

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22. Flexner, S., and Amoss, H. L.: Jour. Exper. Med., 1917, **25,** 539.
23. Amoss, H. L.: Jour. Exper. Med., 1914, **19,** 212.
24. Flexner, S., et al.: Jour. Exper. Med., 1913-1917, **18-25,** inclusive.
25. Mathers, George: Jour. Am. Med. Assn., 1916, **67,** 1019; Jour. Infect. Dis., 1917, **20,** 113.
26. Rosenow, E. C.; Towne, E. B., and Wheeler, G. W.: Jour. Am. Med. Assn., 1916, **67,** 1202.
27. Nuzum, J. W., and Herzog, M.: Jour. Am. Med. Assn., 1916, **67,** 1205.
28. Nuzum, J. W.: Jour. Am. Med. Assn., 1916, **67,** 1437

Depending on variations in artificial cultivation, the micro-organism appears to grow large or small. "The larger forms," according to Rosenow, "tend to grow smaller, so that frequently at the end of twelve or fourteen days, nothing but the tiny globoid bodies, single, in pairs, chains and clumps could be found in the same tubes. After about three weeks, the organism became both larger and smaller; the small forms get beyond the limit of visibility, and nothing but rather large oval cocci staining a pinkish tint with the Giemsa stain are seen." The globoid bodies, Rosenow concludes, are the form which this polymorphous streptococcus assumes under anaerobic conditions.

Rosenow and Towne,[29] in a more recent study, assert that the globoid bodies which Flexner and his associates have considered to be the cause of poliomyelitis are produced by fission of the diplococcus recently isolated.

Rosenow, Towne and Wheeler[30] record an experiment indicating the protection of a monkey against ordinary poliomyelitic virus by the injection of their organism (under conditions which apparently exclude the possibility of any of the globoid bodies being present).

The Rockefeller workers are unwilling to concede that the micro-organism described by these various investigators bears any causal relationship to poliomyelitis.[31]

Amoss,[32] in a renewed study of the globoid bodies, contends that "while a variety of ordinary bacteria has been obtained by various workers, the globoid bodies represent a peculiar species, and thus far alone have sufficed to produce typical poliomyelitis in monkeys by intracerebral inoculation."

Bull[33] insists that the organism described by these various investigators is a streptococcus and that the lesions experimentally produced by its injection are in no way identical with those seen in poliomyelitis. These conclusions he reaches from an experimental study of the inoculation of several species of laboratory animals with cultures of ordinary streptococci and with cultures of streptococci obtained from poliomyelitic sources. Some of the animals developed meningitis with metastatic lesions elsewhere, referable to the streptococcus. "No distinction in the character or frequency of the lesions could be determined between the streptococci derived from poliomyelitic patients and from other sources."

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29. Rosenow, E. C., and Towne, E. B.: Jour. Med. Research, 1917, **36,** 175.
30. Rosenow, E. C.; Towne, E. B., and Wheeler, G. W.: Jour. Am. Med. Assn., 1917, **68,** 280.
31. Editorial: Jour. Am. Med. Assn., 1917, **68,** 1122.
32. Amoss, H. L.: Jour. Exper. Med., 1917, **25,** 545.
33. Bull, C. G.: Jour. Exper. Med., 1917, **25,** 557.

Milton J. Rosenau[34] succeeded in transferring the poliomyelitic virus (using ordinary virus) from rabbit to rabbit through eight successive generations. He obtained positive results in twenty-two out of fifty-four inoculated in various ways. He found that young rabbits were more susceptible to the infection than older ones. Rosenau observes that "the lesions while definite and consistent throughout the series, lack the distinctive features of the pathologic picture of poliomyelitis in man and the monkey."

Gauss[35] confirms Nuzum's findings of a micro-organism in the cerebrospinal fluid of patients with poliomyelitis. As controls, Gauss cultured the cerebrospinal fluid obtained from fifty patients having "scarlet fever and associated exanthems," but in none of these did he obtain the organism mentioned.

Abramson[36] states that in the recent epidemic in New York, the Health Department laboratories there "cultured upward of 1,200 fluids from patients with acute poliomyelitis in all stages of the disease. The medium used was 1 per cent. glucose ascites agar under aerobic conditions. Except for a few evident contaminations, cultures remained sterile."

Kolmer[37] cultured various tissues obtained from cases of poliomyelitis. He isolated four varieties of bacteria, a streptococcus, a diplococcus, diptheroids and gram-negative bacilli. He was unable to produce paralysis by animal inoculation with the organisms isolated.

From specimens of brain and cord tissue taken from poliomyelitic sources, Greeley[38] cultivated a pleomorphic organism which he was able to transmute from a streptococcuslike form to a bipolar bacillus. Cats and rabbits were intravenously inoculated, the results varying from "symptoms analogous to those described as cat distemper by the veterinarians" to degrees of paralysis of various muscles.

Hektoen[39] summarizes the status of the recent findings in regard to their bearing on the etiology of poliomyelitis as follows:

> The micrococcus recently found in poliomyelitis and in poliomyelitis monkey virus appears to have many properties in common with the virus of the disease and with the minute organism described by Flexner and Noguchi. Under the conditions in which this minute organism was grown, the coccus appears to grow much in the same way and to assume very minute forms; the coccus readily passes the filters commonly used in the study of poliomyelitis virus, but the very important question, whether it will pass the finest filters that are said to let the active agent in the virus go through, has not been detetrmined; like the

34. Rosenau, Milton J., and Havens, L. C.: Jour. Exper. Med., 1916, **23,** 461.
35. Gauss, H.: Jour. Am. Med. Assn., 1917, **68,** 779.
36. Abramson, H. L.: Jour. Am. Med. Assn., 1917, **68,** 546.
37. Kolmer, J. A.; Brown, C. P., and Freese, A. M.: Jour. Exper. Med., 1917, **25,** 789.
38. Greeley, Horace: Med. Record, New York, 1917, **91,** 56.
39. Hektoen, L.: Boston Med. and Surg. Jour., 1917, **176,** 687.

virus the coccus under certain conditions is strongly resistant to the prolonged action of glycerol; in monkeys, injections of the coccus three to four culture generations removed from the primary culture have produced conditions absolutely indistinguishable, clinically and anatomically, from the classical induced poliomyelitis in this animal, but the possibility that what may prove to be the true agent of poliomyelitis may be carried along with the coccus under such conditions, must be considered; in young rabbits the coccus causes a flaccid paralysis and also other nervous symptoms, as well as lesions that correspond almost completely to lesions regarded as distinctive of poliomyelitis; but the crucial confirmation test of production of poliomyelitis in monkeys by inoculation of cultures or other materials from such rabbits is still largely lacking; like the active agent in poliomyelitis virus, the coccus, too, is strongly neurotrophic, and in the human disease, as well as in the inoculated rabbit and monkey, it locates with what seems a special preference in the central nervous tissues, in microscopic preparations of which it is demonstrable without great difficulty and from which it can be obtained in culture.

To conclude: The exact significance of this coccus in epidemic poliomyelitis cannot be determined now. The number of cases studied for its presence is too small to permit the conclusion that it occurs constantly in the disease or any form of the disease; in the few instances in which injections of cultures have resulted in a condition indistinguishable from what is accepted as poliomyelitis in the monkey, the possibility that another and more important microbe may have been present cannot be excluded; the true poliomyelitic nature of the very interesting lesion caused by the coccus in rabbits has not been confirmed by proper tests on monkeys; and we lack also the results of extended immunization experiments. In any event, a most interesting coccus has been found that merits study for its own sake as well as on account of the close relation its brief history bears to poliomyelitis.

SYMPTOMATOLOGY

According to Flexner,[5] the incubation period of poliomyelitis "is subject to wide limits of fluctuation. In certain instances it has been as short as two days; in others it has been two weeks or possibly even longer. But the usual period does not exceed about eight days."

Neustaedter[40] speaks of a case in which an incubation period of one day was established. "It was in a physician's child and the father brought the infection after staying in the house of a relative with a poliomyelitis patient for thirty-six hours. Twenty-four hours after he had arrived home, his child was stricken with fever, which lasted two days. On the third day, the child's lower extremities became paralyzed."

While Wickman's classification of eight types of poliomyelitis has generally formed the basis of the presentation of the symptomatology of poliomyelitis, the classification of Peabody, Draper and Dochez is much simpler.[41]

These are:

1. The abortive group.
2. The cerebral group.
3. The bulbospinal group.

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40. Neustaedter, M. N.: New York Med. Jour., 1916, **104,** 145.
41. Bulletin, Dept. Health, City of New York, 1916, **5,** 217.

Ruhräh[42] further subdivides the abortive group into five classes, four of which are given by Wickman, as follows:

1. Those with a course of a general infection.
2. Those showing meningeal irritation.
3. Those with marked pains suggesting an influenza.
4. Those with gastro-intestinal disturbances.

To these he adds,

5. The anginal form, those beginning with a sore throat.

The classification suggests the extremely varied manifestations of this disease. Many observers do not favor the use of the term "abortive"; epidemiologists, on the ground that the term minimizes the equal importance of this type in the transmission of the disease; clinicians, that poliomyelitis should in any of its forms be recognized as an acute infectious disease, which may or may not be associated with paralysis. Emerson suggests the terms preparalytic, nonparalytic and paralytic.

Draper[43] makes a very interesting grouping of the disease, according to its clinical course:

> The first group, called the dromedary group, shows the curious phenomenon of two different periods of illness with an interval of wellbeing. In the second group this period of comparative wellbeing is not present, but there is a sustained period of indisposition of varying intensity. This is called the straggling group. In the third group only do we have all signs pointing from the start to meningeal and nervous involvement. This we called the sudden onset group. A striking thing is that the second portion of the first two groups is very similar to the whole course of the sudden onset group.
>
> In the first two groups there develops a picture of general systemic infection from which the child appears to recover completely, or in part, and then to receive a second blow directly on the cerebrospinal tract. Because of the two distinct groups or humps of symptoms, the analogy to the arrangement of the dromedary's back was taken to express the type figuratively. The temperature curve often shows two elevations, but the figure refers to all the signs and symptoms of each group or hump, whether or not there is a rise of temperature in both. The total duration of the combined phases may vary from a few hours to many days, while the intensity of either phase, the systemic or the meningeal, may touch the extreme of violence or such mildness as to escape detection. In the systemic stage, or first hump, of a well-marked case the clinical picture is that of almost all of the acute infections of childhood—a flushed, uncomfortable, feverish child; in the meningeal stage, or second hump, there are added the special signs and symptoms of meningeal irritability. It becomes at once obvious that the so-called "abortive" types are in all probability examples of the disease in which the first stage or hump constitutes the entire course of the malady, the meningeal stage either never occurring, or, if it does, in so slight a form as to pass unrecognized. The term "abortive" consequently gives a wrong impression, for the termination of the disease at the end of the systemic phase is the more usual occurrence. It would be more correct to speak of acute poliomyelitis, with or without paralysis.

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42. Ruhräh, J.: Am. Jour. Med. Sc., 1917, **153,** 178.
43. Draper, G.: Jour. Am. Med. Assn., 1917, **68,** 1153.

Draper interprets these periods in the cycle of poliomyelitis infection as analogous with the primary lodgment of the virus in the spleen and bone marrow and its subsequent entrance into the cerebrospinal spaces, as illustrated experimentally in monkeys by Flexner and Amoss.[44] The first febrile period of the dromedary or straggling type would correspond to the first part of this cycle, the second hump of the dromedary type to the fixation of the virus in the central nervous system. Draper further says:

> Experiment has shown that the virus gains entrance with difficulty to the central nervous system tissues of monkeys subjected to intravenous inoculation. In human subjects the number of cases recognized as never giving the slightest indication of central nervous system invasion is steadily growing with our experience.
>
> In families in which a frank paralysis case occurs, there are found so frequently other children who present persistently the same symptoms which the paralyzed child has shown in the preliminary hump, that one is led to suppose that these may be examples of infection in which no penetration of the meninges occurred.
>
> In the straggling group the same interpretation applies, the only difference being that the individuals present a continuous course with a fusion of the symptoms of the two stages. Sudden onset cases may be looked on as examples of the malady in which the systemic stage has been overlooked because of its triviality. In this group the spectacular and violent picture of meningeal disease dominates and drives the memory of the slight preceding indisposition from the mother's mind. It is difficult under these circumstances to get from the family any history of the child being unwell during the preceding days.

All observers note the occurrence of fever as the most constant initial symptom. Fischer[45] states that the fever usually persists from three to five days, though it may last from seven to fourteen days. In severe forms, a sudden rise occurs, lasts about forty-eight hours and declines by crisis. These is no characteristic febrile curve that is pathognomonic of poliomyelitis.

Neustaedter[40] considers "the paleness of nasopharyngeal mucosa and its edema, accompanied in the early stage by a serous and frothy transudate, as constant and pathognomonic of the earliest prodromal stage."

Colliver[46] gives a table of the early symptoms. He mentions:

1. Changes in disposition.
2. Fever and anorexia, with constipation or diarrhea.
3. Lack of coordination.
4. Hypersensitiveness of skin.
4. Drowsiness.
6. Pain.

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44. Flexner, S., and Amoss, H. L.: Jour. Exper. Med., 1914, **20,** 249.
45. Fischer, L.: Med. Rec., New York, 1917, **91,** 52.
46. Colliver, J. A.: Arch. Pediat., 1917, **34,** 263.

7. Tremor of certain groups of muscles.
8. Hyperacusis in the bulbar cases.

Koplik[47] reviews the clinical histories of the representative types of the disease. He describes the so-called abortive type. This type can be recognized so as to leave no doubt as to its distinct identity.

A child of 5 years is attacked with a headache, slight malaise and an attack of vomiting lasting five days, intense pain in both lower extremities radiating to the soles of the feet and worse at night, slight pain in the nape of the neck, lassitude, cerebellar gait on walking, increased reflexes in the lower extremities, and rectal temperature above 100.5 F. In ten days the pains have disappeared the child is well and wants to go out and play. The abortive cases present prodromes such as headache, weakness, diminished reflexes and pain in the nape of the neck with or without vomiting and fever; still do not present paralysis, and the patient recovers.

The spinal or bulbospinal type is the most common, and gives the disease its name. Its symptoms are now well known and well defined.

Draper considers the "spine sign" as one of great value in early diagnosis. This consists in an attempt to flex the spine forward. Any such manipulation produces pain and is resisted by the patient.

Fischer[48] considers Colliver's sign as one of the valuable preparalytic evidences of the disease. This is "a peculiar twitching, tremulous or convulsive movement. It usually affects a part or whole of one or more limbs, the face or jaw. It may also affect the whole body."

Gordon[49] calls particular attention to the examination of the reflexes in the early diagnosis of suspicious cases. The patellar and achilles reflexes should be investigated. Even a diminution of these reflexes should put one on guard for this disease, particularly during an epidemic.

Sheffield[50] notes the frequent onset of poliomyelitis with sore throat, "the tonsils presenting either simple congestion or also small greyish-white deposits." When such symptoms are associated with a palatal paralysis, the picture of diphtheria may be closely simulated. The early symptoms of the disease may suggest laryngeal diphtheria,[51] appendicitis,[52] bronchopneumonia,[53] or may duplicate any meningeal disease. While all observers agree that many cases occur which remain undiagnosed, during an epidemic the diagnosis is apt to be made with-

47. Koplik, H.: Jour. Am. Med. Assn., 1916, **67,** 310.
48. Fischer, L.: Med. Rec., New York, 1916, **90,** 194.
49. Gordon, A.: New York Med. Jour., 1916, **104,** 583.
50. Sheffield, H. B.: Med. Rec., New York, 1916, **90,** 330.
51. Polozker, I. L.: Jour. Michigan Med. Soc., 1917, **16,** 100.
52. Le Boutillier, T.: Am. Jour. Med. Sc., 1917, **153,** 188.
53. Louria, L.: Arch. Pediat., 1916, **33,** 853.

out justification. Thus the Harvard Infantile Paralysis Commission[54] report that of the 187 calls received, only 123 proved to be poliomyelitis. The remaining sixty-four instances embraced many diseases (infectious diarrhea, gastro-enteritis, influenza, vaccination, hysteria, tuberculosis, "mild digestive upsets," "nervousness"). Among this group there were also four cases of meningitis — two of the epidemic type, one tuberculous and one luetic.

Wilson[55] classifies the prominent prodromal symptoms, based on a study of 400 histories of patients with poliomyelitis admitted to the Willard Parker Hospital. Fever was present as an initial symptom in 334 cases. Only 2 per cent., on careful investigation, gave no history of fever. Vomiting was an initial symptom in sixty-seven cases, as an early symptom in 132 cases. "One hundred and fifty-six cases gave a definite history of persistent constipation for two or more days, resisting ordinary catharsis." Persistent drowsiness was noted in 72 per cent. of the cases. Other nervous symptoms observed were irritability, hyperesthesia, tremor, delirium, convulsions. Profuse sweating was noted in forty-five cases. This was usually out of proportion to the fever present. Wilson considers a careful history as suggestive, particularly during an epidemic.

Neal and Dubois[56] record two cases of poliomyelitis associated with blindness. In one instance, sight was restored at the end of about three months. The second instance was a more recent one in which the blindness was still present at the time of their report.

No characteristic eye signs have occurred in poliomyelitis, according to Hansell.[57] The eye complications varied considerably as one would expect following such a generalized cerebrospinal infection.

It seems to be generally agreed that the examination of the cerebrospinal fluid in poliomyelitis offers the most useful single procedure available in the early diagnosis of the disease.

Abramson[58] mentions the usual findings as follows:

1. Fluid is increased and under pressure.
2. Fluid is clear as a rule, but may be opalescent.
3. Albumin and globulin increased.
4. Fehling's solution reduced in the majority of instances.
5. Cells increased.
6. The predominating cell type is the small, mononuclear, which may constitute 90 per cent. of the cells present. In opalescent fluids

54. Report Harvard Infantile Paralysis Commission, Boston Med. and Surg. Jour., 1917, **176,** 637.

55. Wilson, May G.: Am. Jour. Dis. Child., 1917, **13,** 506.

56. Neal, J. B., and Dubois, P. L.: Am. Jour. Med. Sc., 1916, **152,** 313.

57. Hansell, H. F.: Am. Jour. Dis. Child., 1917, **13,** 516.

58. Abramson, H. L.: Med. Rec., New York, 1916, **90,** 793.

one may find the polynuclears increased, as high as 75 per cent. Abramson has also noted the presence of glialike cells and endothelioid cells.

Zingher[59] thinks the cerebrospinal fluid quite characteristic even in its early stages. He says:

> There is an increase in the total number of cells, from twenty to 600 or more. These cells are mostly lymphocytes, with a small proportion of large mononuclear and polynuclear cells. During the earliest stages of the disease there may be a transient relative and absolute polynucleosis. There is an increased amount of albumin, globulin and substance which reduces Fehling's solution. Often on the surface of the spinal fluid, as it is being drawn into a test tube, a thin filament of fibrin appears, which breaks up into small flakes when the fluid is gently shaken.

Zingher describes what he terms a ground-glass appearance when such fluids are viewed by transmitted light. The suggestion of ground glass is due to the increased number of cells in the fluid. This appearance is not present in a fluid that has been standing several hours. The same author speaks of a so-called "foam test." All spinal fluids when shaken in a test tube create a foam, but that formed by shaking a test tube half filled with spinal fluid from a poliomyelitic patient is much denser and more persistent. Zingher warns against deductions with a spinal fluid that is not absolutely free from blood.

Josephine B. Neal[60] discusses the laboratory aids in the diagnosis of poliomyelitis. Most evidence furnished by such procedures as are available are of a corroborative nature and not absolutely diagnostic. The neutralization test is too complicated. In this test, a mixture of a fatal dose of an active virus with the suspected fluid, obtained during the stage of recovery, is incubated and injected intracerebrally into a monkey. Failure of the disease to develop indicates neutralization of the virus. The examination of the cerebrospinal fluid helps differentiate from the early stages of meningitis and from meningismus. Large monoculear cells, which may have some diagnostic significance, are occasionally noted. "Two rare types of spinal fluids sometimes occur in poliomyelitis when the hemorrhagic process has been more than usually extensive. The first of these is of true hemorrhagic character, the red blood cells being evenly diffused throughout the fluid. When collected in successive tubes, the specimens are all homogeneous, showing no change in the intensity of the hemorrhage. This serves to differentiate it from bloody fluids obtained by the accidental puncture of a vein. The second of these rarer fluids illustrates the so-called syndrome of Froin. It has a characteristic yellow color and coagulates

59. Zingher, A.: Jour. Am. Med. Assn., 1917, **68,** 817.
60. Neal, Josephine B.: New York Med. Jour., 1916, **104,** 167.

spontaneously." These fluids mentioned are not pathognomonic of poliomyelitis.

In the diagnosis of poliomyelitis, Dubois[61] considers the laboratory more of value "by what it rules out." The important features are the increased cell count, which may be "marked, moderate or slight," the positive globulin and the reduction of Fehling's solution. Frequently cells are so degenerated as to make differential classification difficult.

Among the examinations of cerebrospinal fluid made by the Harvard Paralysis Commission[54] there were thirty-one instances of fluids from patients who were ultimately proven not to have poliomyelitis. In two instances the cell count was 12 and 15, respectively. In all other instances the cell count was below 10. In the positive cases, the count ranged from 34 to 1,980 per cubic millimeter.

Felton and Maxcy[62] find the colloidal gold reaction an aid in the laboratory diagnosis of poliomyelitis. The fluids were taken from patients in various stages of the disease. "The gold chlorid curve given in these cases is singularly constant and occurs in the so-called luetic zone." After the subsidence of the acute illness the reaction may be most prominent in the "meningitic zone."

Jeans and Johnson[63] also applied the gold-chlorid test, with very similar results, the reaction occurring in the lower dilutions. Even when a reaction does take place in the middle or meningitic zone, it will not be restricted to this particular zone, but also embrace the first zone.

Hoyne and Cepelka[64] record the leukocyte counts in thirty patients with poliomyelitis. Leukocytosis was the rule and usually persisted for at least two weeks.

PROGNOSIS

Prognosis is a hazardous venture, according to Abramson.[58] Cases which appear grave may clear in twenty-four to forty-eight hours and present the most astonishing improvement. There are others which appear mild, develop fulminating symptoms and the patients die in a few hours. In adults, the disease seems more violent. Relapse occasionally occurs after a period of apparent improvement.

In Weisenburg's experience,[65] "the mildest cases often developed the severest infection, while a very sick child might have only limited paralysis." The most fatal cases in his experience were those of the so-called Landry type.

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61. Du Bois, Phoebe: Arch. Pediat., 1916, **33**, 856.
62. Felton, L. D., and Maxcy, K. F.: Jour. Am. Med. Assn., 1917, **68**, 752.
63. Jeans, P. C., and Johnson, M. R.: Am. Jour. Dis. Child., 1917, **13**, 239.
64. Hoyne, A. L., and Cepelka, F. P.: Jour. Am. Med. Assn., 1916, **67**, 666.
65. Weisenburg, T. H.: Jour. Am. Med. Assn., 1916, **67**, 1872.

La Fetra[66] warns that one should be particularly cautious in giving an absolutely good prognosis in cases of facial paralysis.

Ruhräh[42] says that "the severity of the initial symptoms bear no relation whatever to the course of the disease, as one sees a very mild onset followed by most extensive paralysis and even death, and other cases coming in a most fulminating manner which subsequently clear up entirely."

The case mortality in this epidemic was much higher than that of previous ones. In New York City, it reached 26.96 per cent. In New York State, not including the city, it was 21 per cent.[2] The younger the child, the higher the mortality rate.

Partial statistics available at present give variable figures as to the percentage that escape paralysis. The general impression exists that there are a large number of such instances, which probably remain undiagnosed. In one period of six weeks during the New York epidemic, in an analysis of 2,053 cases of patients discharged from the hospitals under the control of the New York Health Department,[67] it was stated that 66 per cent. showed some paralysis; 15 per cent. had never had paralysis, and 15 per cent. showed a disappearance of previously existing paralysis. The last figure will exhibit a proportionate increase with the length of intervals following the acute infection.

Lovett and Martin[68] have devised a spring balance test by which the efficiency of any muscle or group of muscles may be measured and expressed in percentages. With the patient in a certain standard position, the test is performed by having the patient hold a position against the pull of a spring balance. The resistance exerted represents the muscular strength. By the use of this test these observers have determined that the distribution of the paralysis is much more general than has been ordinarily supposed; that cases of so-called abortive paralysis are often cases in which the paralysis is of too mild a degree to be detected by the usual methods of examination; that the proportion of partially paralyzed to totally paralyzed muscles is about 9 to 1. They also demonstrated that spontaneous improvement occurs for a much longer period and to a greater degree than has generally been thought possible.

Sayre[69] and others doubt the significance of the reaction of degeneration, since despite the presence of the reaction of degeneration, muscles may regenerate.

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66. La Fétra, L. E.: Arch. Pediat., 1916, **33,** 865.
67. Medical News: Jour. Am. Med. Assn., 1916, **67,** 1236.
68. Lovett, R. W., and Martin, E. G.: Jour. Am. Med. Assn., 1916, **66,** 729. Lovett, R. W., and Martin, E. G.: Am. Jour. Orthop. Surg., 1916, **14,** 415.
69. Sayre, R. H.: New York Med. Jour., 1916, **104,** 1029.

TREATMENT

Inasmuch as the epidemiologic knowledge of this disease is incomplete, the prophylactic measures which are advised are such as apply to other communicable diseases.

"Of first importance," says Emerson, "is the more general recognition by practitioners of nonparalytic cases through clinical observation and laboratory procedures."

Emerson offers an outline of necessary administrative measures for the control of the disease as follows:

1. The requirement that all recognized and suspected cases be promptly reported.

2. Isolation of patients in screened premises. The duration of infectivity being unknown, the period of isolation must necessarily be arbitrary. Six weeks has been recommended by the Conference of State and Territorial Health Officers with the Surgeon-General of the Public Health Service as sufficient, and this period has been generally accepted throughout the United States.

3. Disinfection of all body discharges.

4. Restriction of the movements of intimate associates of the patient, so far as practicable. This should include at least exclusion of the children of the family from schools and other gatherings.

5. Protection of children, so far as possible, from contact with other children or with the general public during epidemics.

6. Observations of contacts for two weeks after the last exposure.

Interstate and intrastate quarantine regulations which at the height of the 1916 epidemic in some instances bordered on the hysterical, have now been placed on a uniform basis.[70] In August, 1916, a special conference of state and territorial health officers met with the United States Public Health Service for the consideration of measures for prevention of the spread of poliomyelitis. The transactions of this conference are available in a Public Health Service publication.[71]

Since the nasopharynx is generally believed to be the point of entry for the virus of poliomyelitis, Bryant[72] recommends measures for the routine treatment of the nasopharynx. The correction of any nasal disturbance and the use of various antiseptic and astringent solutions forms the basis of the treatment. Hydrogen peroxid, silver salts and the salts of iron are among the local remedies advised.

Whittemore[73] suggests the insufflation of the nose and throat with kaolin as advised for diphtheria carriers by Hektoen and Rappaport.

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70. U. S. Public Health Reports, Reprint 361.
71. U. S. Public Health Bull. 83.
72. Bryant, W. S.: New York Med. Jour., 1916, **104,** 727.
73. Whittemore, W. S.: Boston Med. and Surg. Jour., 1916, **175,** 231.

Roper[74] discusses the advisability of tonsillectomy, since Rosenow claims that the tonsil may harbor the offending organism.

Emerson voices the opinion of many others in some remarks regarding treatment. He says:

> There is no specific treatment of established value in poliomyelitis. During the persistence of the acute symptoms of the disease, the important principles of treatment are rest in bed, symptomatic relief and passive support for the prevention of deformities. Active measures during this stage are not only useless, but are apt to cause serious and often permanent injury. Hospitalization of patients where possible is to be encouraged. The best chances of recovery from residual paralysis demand skilful after-care, often long continued, and always under the direction of a physician familiar with the neurologic and orthopedic principles of treatment. The provision of such after-care often becomes a community problem, demanding the cooperation of all available agencies, social and professional.

While lumbar puncture affords the best single therapeutic agent, some cases showed good recoveries without any other than expectant treatment. Many think that the good results reported by the use of various intraspinal measures are in the main attributable to the lumbar puncture per se.

SERUM THERAPY

Flexner and Lewis have shown that monkeys that recover from poliomyelitis are immune to subsequent inoculation with the virus of the disease. This was later shown to be due to the presence of neutralizing substances in the blood of such animals. It was also demonstrated that the blood serum of an individual that has recovered from poliomyelitis possesses similar neutralizing principles. By utilizing immune serums, Flexner and his co-workers were able to prevent the occurrence of paralysis in infected monkeys. The application of this measure in the treatment of epidemic poliomyelitis in man was first made by Netter.[75] He employed the serum of individuals who had had the disease at some previous time—even as long as thirty years previously.

Flexner[76] discusses the application of this method. He says:

> The dose of the serum, which must, of course, be sterile, but need not be inactivated, should be determined by the age of the patient, and will, in part, be determined by the quantity of serum available. Probably doses ranging from 5 to 20 c.c. will be found suitable, the injection to be repeated several times at twenty-four-hour intervals according to clinical conditions and indications. The effects of the immune serum should be sought in the checking of the progress of the disease, namely, the prevention or minimization of the paralysis when employed in the preparalytic stages, and the arrest of its extension when used in progressing paralytic conditions. Since the immunity sub-

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74. Roper, J. C.: Med. Rec., New York, 1916, **91,** 1139.
75. Netter, A.: Bull. de l'Acad. de méd., Paris, 1915, **74,** 403.
76. Flexner, S.: Jour. Am. Med. Assn., 1916, **67,** 583.

stances have been determined by neutralization tests to persist in the blood for many years, it is probable, as Netter had indicated, that persons who have passed through an attack of poliomyelitis many years earlier may be utilized as sources of the serum; reasoning from analogy, it would probably be advantageous to prefer persons whose attack was less remote so as to insure as high concentration of the immunity bodies as possible. The conditions surrounding the injection of the serum into the meninges are identical with those observed in the analogous case of epidemic meningitis. Before each dose of serum is injected a suitable quantity of the cerebrospinal fluid is to be withdrawn, and the injections should be made slowly. In choosing the person who is to serve as the source of blood from which the immune serum is to be derived, precaution should of course be taken to secure a healthy donor; it would be advisable to fortify the usual clinical examination by a Wassermann test.

Zingher[59] describes the methods of obtaining and preparing serum from immune donors. He receives the blood in small square bottles in quantities of 1 to 2 ounces; the bottles are slanted to allow larger surface for clotting and separation of serum. The serum is centrifuged, and may then be preserved by the addition of 0.2 per cent. trikresol solution. (This may increase the irritant effect of the serum.) After standing in the icebox for forty-eight hours, a sediment which forms on the addition of trikresol is removed and the serum is passed through a Berkefeld filter and bottled. When these facilities are not obtainable, the serum may be defibrinated and centrifuged, or the serum separated in the usual way and used immediately. No inactivation of serum is necessary.

Zingher tabulates the results from the use of serums obtained from individuals who had had the disease at intervals varying from a couple of months to over thirty years previously. He did not observe any difference in the results obtained. Indeed, Zingher considers it problematic whether such results as are obtained may not be due to the cellular response created by the intraspinal injection of a protein, and therefore not a specific one. Of fifty-four preparalytic cases treated with immune serum, forty-four patients remained free from paralysis, and of the remaining ten, five made a complete recovery. Of ten patients treated with normal serum, nine remained free from paralysis and one died. Among the paralytic cases the mortality was high despite the use of serum, which Zingher explains on the ground of the extreme severity of these cases. There were forty-five deaths in a total of 119 patients treated.

Schwarz[77] treated twenty-one patients with serum and a similar number by the expectant plan. Of the former, nine recovered without paralysis. Of the latter, seventeen recovered without paralysis.

Petty[78] reports eleven patients treated by subdural administration of immune serum. Striking results were not obtained.

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77. Schwarz, H.: Arch. Pediat., 1916, **33,** 859.
78. Petty, O. H.: New York Med. Jour., 1916, **104,** 1190.

In a series of patients treated by the Harvard Infantile Paralysis Commission, there was no evidence of paralysis in 69 per cent. of the total number seen in the preparalytic stage. In a series of eighty-five cases furnished them by Draper, in which no serum was used, 56 per cent. developed no paralysis. The difference is not sufficiently striking to warrant any definite conclusions.

Sophian[79] was unable to note any greater advantages from the use of immune serum than from normal horse serum.

Wells[80] thinks that the best results are obtained by combined intravenous and intraspinal injections. The intravenous route has the advantage of the utilization of a much greater amount of serum, and, according to Wells, is a logical procedure, because the peculiar distribution of poliomyelitic lesions suggest a hematogenous infection.

Draper[43] discusses the apparent discrepancies between statistical proofs of the use of immune serum and the clinical impressions received. On the basis of the analogy drawn by Draper between the two "humps" of the clinical picture and the interception of the infecting virus by the spleen and meninges, the use of any serum, homologous or otherwise, should theoretically await the onset of meningeal symptoms. Since the clinical recognition of this onset is not always a simple matter, the delay in the use of serum may mean the loss of valuable time. Since Flexner and his associates have shown experimentally that the injection of serum intraspinally renders an animal more susceptible to an injection of poliomyelitic virus, the entire procedure may be a dangerous one. In the final decision, each case must be considered by itself.

Amoss and Chesney consider the use of serum a procedure of definite therapeutic value. When given under suitable conditions, its administration is harmless. They recommend that it be used during the first thirty hours of the disease, and advise the administration of large doses, utilizing the intravenous and intraspinal routes. According to their studies, the serum is more efficacious in preventing paralysis than in effecting its retrogression.

Flexner and Amoss[81] present an interesting study explaining the alleged beneficial results derived from the intraspinal injection of normal serum in poliomyelitis. They demonstrate that the injection of any serum increases the permeability of the meninges. This would allow the passage of any neutralizing principles from the blood to the cerebrospinal fluid. Since in the very early stages of the disease, immunity principles do not exist in detectable amounts in the blood,

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79. Sophian, A.: Jour. Am. Med. Assn., 1916, **67,** 427.
80. Wells, C. W.: Jour. Am. Med. Assn., 1916, **67,** 1211.
81. Flexner, S., and Amoss, H. L.: Jour. Exper. Med., 1917, **25,** 499.

the rationale of the use of normal serum comes into question. On the same basis the use of immune serum is an obviously rational procedure, and may prove curative.

Rueck[82] reports three cases of poliomyelitis treated successfully by transfusion of the citrated normal blood of adults.

Duncan[83] reports the use of the patient's own spinal fluid for intramuscular injection. He removed 10 c.c. by lumbar puncture and injected 1 c.c., and later 0.5 c.c. more, intramuscularly. The patient recovered.

Meltzer[84] objects to the method as irrational and dangerous.

Ager[85] replies to Meltzer's criticism. He says that in the use of the method as supervised by him, 60 to 70 c.c. of spinal fluid were removed and only 0.5 to 3 c.c. reinjected. There were no bad results. Some were strikingly improved. Ager, however, is skeptical about its ultimate value or that of any present method of treatment. He believes that the only method of value will be the production of a concentrated serum from an immunized lower animal.

Neustaedter and Banzhaf[86] report some neutralization experiments obtained by the use of an antipoliomyelitis horse serum. Since previous investigators had not been successful, he attempted to immunize horses by injections of the filtrates of brain and cord (from human poliomyelitic sources) which had previously been incubated with a proteolytic ferment. This was done in order to obtain a possible endotoxin. The neutralization experiments were positive without exception.

Nuzum[87] reports the production of a poliomyelitic antiserum. He immunized sheep by successive injections of the organisms he previously described as the causative agent in the disease. The antiserum prepared contained agglutinins, opsonins and complement fixation bodies as well as antibactericidal properties. Its therapeutic possibilities have not been ascertained.

Mathers and Tunnicliff[88] report the occurrence of specific opsonin in the blood of convalescent poliomyelitis patients. In conjunction with Dr. Katherine Howell, Tunnicliff has found that "the serum of rabbits immunized against different strains of poliomyelitic cocci contains antibodies in high concentration, which are apparently specific for the poliomyelitic organisms."

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82. Rueck, G. A.: Med. Rec., New York, 1916, **90,** 587.
83. Duncan, C. H.: New York Med. Jour., 1916, **104,** 342.
84. Meltzer, S. J.: New York Med. Jour., 1916, **104,** 477.
85. Ager, L. C.: New York Med. Jour., 1916, **104,** 573.
86. Neustaedter, M., and Banzhaf, E. J.: Jour. Am. Med. Assn., 1917, **68,** 1351.
87. Nuzum, J. W.: Jour. Am. Med. Assn., 1917, **68,** 24.
88. Mathers, G., and Tunnicliff, R.: Jour. Am. Med. Assn., 1916, **67,** 1935.

Meltzer[89] offers an interesting discussion on the treatment of poliomyelitis by the intraspinal injection of epinephrin chlorid and the maintenance of artificial respiration by intrapharyngeal insufflation. Meltzer quotes Peabody, Draper and Dochez as declaring that, "it is often extremely difficult to reconcile the clinical symptoms which are referable to pontine lesions with the actual necropsy findings." Such symptoms, Meltzer assumes, may be due to local edemas which disappear as soon as the circulation stops. Since epinephrin exerts a favorable influence on local edemas, its use in poliomyelitis suggested itself. Meltzer offers the further hypothesis that epinephrin may be specifically antagonistic to the virus of poliomyelitis. The Rockefeller workers have shown that the abdominal sympathetic ganglia exhibit the mildest lesions in experimental infections of poliomyelitis. This suggests the possibility that the nerve tissues are antagonistic to the virus. The adrenal, being one of the chromaffin tissues, may exert a similar influence. He describes the technic of its administration. Two c.c. of a 1 to 1,000 epinephrin solution should be injected intraspinally every four to six hours. "Before the first injection is given, a fairly large quantity of spinal fluid should be withdrawn, the quantity being in proportion to the pressure prevailing in the spinal canal. The subsequent injections should be made without regard to the presence or absence of spinal fluid." The injection is given with 2 c.c. of normal salt solution. If no spinal fluid is present, the epinephrin should be washed in with at least 5 or 6 c.c. of salt solution. "In cases in which the encephalitic symptoms are predominant, it should be used in inverse proportion to the exciting effect which the injections may produce." The injections should be continued for four or five days after all paralysis has disappeared, "or at least until no further reduction in the extent of the paralysis has taken place." Meltzer also advises the administration of oxygen. Absorbed by the blood, and combined with the lipoids of the nervous tissue, it may form an unfavorable environment for the anaerobic poliomyelitic organism.

Lewis,[90] Haas[91] and others report favorable results by the use of epinephrin chlorid intraspinally.

Hoyne and Cepelka[64] say that "some patients showed marked improvement in from one-half to one hour following the epinephrin injection." On several occasions a patient with a totally paralyzed arm would make a voluntary movement of the arm within an hour after receiving the epinephrin. Such marked improvement, however, was

89. Meltzer, S. J.: New York Med. Jour., 1916, **104,** 337.
90. Lewis, P. M.: Med. Rec., New York, 1916, **90,** 540.
91. Haas, S. V.: Med. Rec., New York, 1916, **90,** 425.

seldom permanent, but gradual improvement in some cases seemed to be more rapid."

Bass[92] describes the symptomatic treatment of poliomyelitis. Complete rest of the patient is essential, even if plaster-of-Paris must be used to immobilize. Pain and hyperesthesia are further treated by bromids and opiates. Acetyl salicylic acid may also be used. Local applications of heat are beneficial, though warm baths should not be resorted to, since they occasion unnecessary movements by the patients. The prevention of improper attitudes on the part of the extremities must be carefully watched. Sandbags, adhesive plaster and frames for the bedclothes may be used as preventives.

Charlton Wallace[93] divides the orthopedic treatment into three stages. These are (a) the acute stage, (b) the stage of apparent paralysis, (c) the stage of convalescence. The orthopedic treatment during the first stage is generally aimed at the relief of pain. This is accomplished by absolute rest and immobilization in plaster-of-Paris dressings, supplemented by careful, judicious nursing. Prolonged bed treatment is important in the second stage, lasting two or three months. Daily sponging with alcohol, and skin rubbing to avoid decubitus should not be forgotten. In the bulbospinal type, the patient should be placed on a mattress resting on a fracture board. All movements should be restricted, especially any attempt to sit up. Plaster-of-Paris bandages are indicated to prevent contractures of the feet. The stage of convalescence extends from the beginning of the ambulatory period to the end of the first year. During this time every effort should be made to maintain muscle balance and stimulate the paralyzed muscles. Daily massage and manipulation of the active muscles should be performed. Overbracing is preferable in the early months, after which it is gradually diminished. Electrotherapeutics may be of some value during the first year.

Lovett[94] and many other orthopedists warn against overfatigue. Lovett states that the convalescent patient is allowed up under supervision after two to three months. "Braces bear about the same relation to the treatment of poliomyelitis that crutches do to the treatment of fracture of the leg." If the patient cannot walk without braces, or if in walking, unnatural attitudes are assumed, some form of mechanically sound, light and properly fitted apparatus is advisable. Massage should not be overdone. Lovett emphasizes the importance of muscle training. This consists in having the patient execute special movements, and at the time of the effort, assisting him manually. By such

92. Bass, M. H.: Arch. Pediat., 1916, **33,** 611.
93. Wallace, Charlton: Arch. Pediat., 1916, **33,** 599.
94. Lovett, R. W.: Med. Rec., New York, 1916, **90,** 705.

practices, Lovett believes that new paths will be created to carry motion impulses and thus "reconnect a cerebral impulse with a peripheral muscular contraction." Even in the very chronic cases, muscle training is beneficial. Operative treatment should not be considered for two years.

Whitman[95] notes that muscle training is difficult of application in young children. He urges the better equipment and centralization of the clinics that deal with the after-treatment of poliomyelitis.

Ashley[96] says that muscle training should be in skilled hands. He considers massage very useful if not overdone. Parents may be instructed how to give it. "Electricity," according to Ashley, "is a good placebo when administered with a weak current. Its best and legitimate use will be to bring the patient for frequent regular examination, once in seven to ten days, in order that the physician may keep the child under observation and combat early any tendency to deformity."

Sayre[69] advises the use of strychnin during the convalescent stage. Local application of heat is also beneficial. Sayre notes that in regard to the use of electricity, the pendulum has swung from enthusiastic advocacy to absolute skepticism.

Frauenthal[97] is enthusiastic about the value of electricity. He begins its use when paralysis first appears. The high frequency current may be used along the spine for ten minutes every three hours for three days, during the acute stage. In the treatment of the paralysis, Frauenthal thinks that electricity maintains the tone and function of the muscles. "The least possible amount that will produce a contraction should be used." The slow wave sinusoidal current is the most perfect current to use, since it is best borne by young children. He applies sponge electrodes at the origin and insertion of the muscle needing stimulation. Frauenthal also advises light massage and baths while the patient is in quarantine.

Orthopedists generally emphasize the importance of rest and absolute quiet during the first two or three months, and the institution of orthopedic measures only to prevent deformity. During the second period (after the third or fourth month) they uniformly advise the use of light massage and muscle training, warning against carrying such measures to the point of fatigue. The value of electricity is considered very much overestimated. As a general thing, no operative measures are advisable during the first two years, but braces and splints

95. Whitman, R.: Med. Rec., New York, 1916, **90,** 1062.
96. Ashley, D. D.: New York Med. Jour., 1916, **104,** 725.
97. Frauenthal, Henry W.: New York Med. Jour., 1916, **104,** 1042; ibid., 1917, **105,** 247.

properly applied may prove useful.[98] Such measures to be successful must be constantly supervised.

Geyser[99] recommends electrotherapy, using it, not to cause contractions, but as a method of applying heat to affected muscles. When the functional response is slow, he advises the use of the sinusoidal current, and later the faradic current and muscle training.

Gaenslen[100] discusses the management of the stationary or paralytic stage. Treatment must be directed toward the maintenance of an equally distributed muscular balance. The factors which influence this balance cannot be controlled by massage and electricity alone. Gaenslen pleads for a careful study of these cases. Bad results are frequently due to neglect and to lack of cooperation on the part of parents.

Ryerson[101] discusses which patients can be improved by apparatus and which by operation. He censures the use of braces and repeated tenotomies in numerous cases in which muscles are paralyzed, resulting in an aggravated condition.

Gallie[102] describes the technic and reports good results with the operation of tendon fixation in deformities allowing poliomyelitis.

Sharpe[103] offers a preliminary report on a method for the restoration of function to paralyzed muscles. This he attempts by the "intradural anastomosis of a nerve root whose motor cells are active to a paralyzed nerve root." He selects active nerves whose function can be dispensed with. The duration since operation in three cases reported is not sufficiently long to speak of results.

Various operative measures for the correction of deformities following poliomyelitis are discussed by orthopedic surgeons.[104]

Bardine[105] and Wright[106] make earnest pleas for proper team work of hospitals and social agencies in the after-care of infantile paralysis. The problem is as much a social one as it is orthopedic.

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100. Gaenslen, F. J.: Wisconsin Med. Jour., 1916, **15,** 148.
101. Ryerson, E. W.: Am. Jour. Orthop. Surg., 1916, **14,** 59.
102. Gallie, W. E.: Am. Jour. Orthop. Surg., 1916, **14,** 18.
103. Sharpe, N.: New York Med. Jour., 1916, **104,** 14.
104. Am. Jour. Orthop. Surg., 1916, **14,** 381.
105. Bardine, O. H.: Med. Rec., New York, 1916, **90,** 1066.
106. Wight, L. O.: New York Med. Jour., 1916, **104,** 585.

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OBSERVATIONS ON THE PRESENCE OF THE BACILLUS ABORTUS BOVINUS IN CERTIFIED MILK

PRELIMINARY NOTES *

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A large amount of experimental work has been done during the past decade to impress on the public and profession the fact that raw milk is never a safe milk, and that in order to be fit for consumption all milk must be pasteurized. The effect has been that in many states legislation has been enacted governing and requiring the pasteurization of all milk with one exception, and this exception is certified milk. In view of the enthusiasm, entirely justified, of public health experts everywhere as to the value of pasteurization, suggestions have been rather numerous, particularly during the past two years, that even certified milk is not a safe raw product, and that it, too, should be heated. Without entering into the relative values of raw and heated milk in infant feeding, it is unquestionably permissible to say that with our present knowledge most pediatrists are still of the opinion that raw milk plays a very important and needed rôle during the first two years of life, provided such a product can be obtained as is not a potential source of danger to the infants consuming it.

It has always been the proud opinion of those medical men interested in the certified milk problem that in this product conditions as ideal as were possible had been met, and that for practical purposes certified milk was a safe raw milk. When the literature, however, began to offer suggestions here and there doubting its efficiency and safety, it became necessary for the problem to be attacked by those interested in it, in order that the foundation on which the movement had been built might be forever strengthened and its value be definitely proved, or, if it was not a dependable product, that this even more important fact should be elicited.

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Within certain human limitations it has always been felt by certified commissions that a very thorough safeguard had been built against the ordinary milk-borne infections due to human contamination by a fairly perfect system of dairy hygiene. The weak link in the chain, therefore, lay in that group of diseases to which man is heir, emanating from the cattle themselves. And in this group bovine tuberculosis plays the leading rôle. Tuberculin testing, performed twice a year, has succeeded in reducing the disease to a minimum, but even with this precaution some reactors are usually present, and occasionally a severe infection will decimate a herd under the best of conditions.

The following question, therefore, suggested itself. By semi-annual tuberculin tests, can we discover reactors so early in the course of their disease that they are not throwing out tubercle bacilli in their milk and in this way disseminating bovine tuberculosis? To determine this fact but one method seemed satisfactory, namely, to inject samples of certified milk into guinea-pigs in an effort to produce tuberculous lesions, if tubercle bacilli were present. A careful review of the literature has failed to show any record of this determination having ever been made with certified milk, although the number of men who have demonstrated the presence of tubercle bacilli in market milk is too large to mention. With this idea in mind, samples of certified milk were collected over a period of several months from the regular distributors so that the product as it was ordinarily consumed should be investigated.

TECHNIC

The following technic was carried out: Eight hundred cubic centimeters of milk were centrifuged for one-half hour, 2,000 to 3,000 revolutions per minute, 100 c.c. in each of eight tubes. At the end of that time the cream and skim milk were poured off and the sediments were collected in about 20 c.c. of normal saline solution. On account of centrifugalization for one-half hour, the high speed, and some experiments of one of us, it was not considered necessary to inject the cream layer, which otherwise frequently retains tubercle bacilli. Five cubic centimeters of the sediment suspended in saline were then injected intramuscularly into the upper and inner surface of the right hind thigh of a guinea-pig. Four guinea-pigs were injected for each sample of milk.

Without giving much thought to the problem when the experiments started, beyond the question as to whether or not tuberculous lesions would be discovered at the time of the necropsy, the animals in the first experiment were not disturbed for about twelve weeks. At this time two of them were chloroformed, and, as is not infrequently the case, in gathering experimental data, a very unexpected situation was discovered. The animals were not appreciably emaciated. On post-mortem examination the spleens were found markedly enlarged and studded with small grayish nodules. There was a general adenopathy, but no caseation. The testes of both animals were atrophic and the

epididymis of one contained pus. The lungs, liver and kidneys were apparently normal. Careful examination of the spleen nodules after maceration failed to show any acid-fast bacilli. We were, therefore, apparently dealing with a disease simulating tuberculosis but having its most marked effect in the spleen, lymph nodes and sex organs. The condition was immediately recognized by one of us as abortion disease of guinea-pigs, and it was evident that we had to deal with two problems, tuberculosis, for the determination of which the experiments were started, and abortion disease, the determination of which the experiments elicited.

The literature pertaining to the subject of this paper as announced in the title has been purposely not even referred to up to the present, because it seemed more logical to state first the object of the work, and then elaborate on the literature after emphasis had been laid on the peculiar manner in which our attention was focused on the positive findings.

In discussing the literature it will be desirable to consider it in the following manner: First, those investigations bearing on milk as a cause of abortion disease; second, those investigations bearing on methods of diagnosis; third, those bearing on the possible result that the presence of these organisms in milk may have on public health.

Ever since Bang,[1] in 1907, fulfilled Koch's laws in regard to the *Bacillus abortus bovinus* as the etiologic agent in abortion disease of cattle, countless investigators have been attacking the problem because of its fascinating biologic possibilities, and on account of its very great economic importance.

Theobald Smith,[2] in 1894, first called attention to a peculiar disease occurring in guinea-pigs, following the inoculation of milk, that resembled tuberculosis, but it was not until seventeen years later, in 1911, that he, in association with Marshal Fabyan,[2] determined beyond question that these lesions were due to *B. abortus*. Their conclusions at this time were:

> 1. *B. abortus* (Bang) is most likely the only cause of infectious abortion among cattle; 2, *B. abortus* produces in guinea-pigs a peculiar general disease that very seldom kills the animal. It resembles tuberculosis and is characterized by chronic interstitial new tissue, consisting for the most part of epithelioid and lymphoid cells; 3, *B. abortus* occurs in milk, and therefore it is indicated to determine whether it can have any causative relationship to sclerosis of tissues or organs, or to the chronic diseases of man or domestic animals.

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2. Smith, Theobald, and Fabyan, Marshal: Ueber die pathogene Wirkung des Bacillus abortus Bang, Centralbl. f. Bakteriol. u. Parasitensk., Abt. I, 1912, **61**, 549.

Schroeder and Cotton[3] state that the udder is the favorite habitat of *B. abortus,* and in the nonpregnant cow it is the only habitat. One animal in their work showed bacilli in her milk for seven years. They injected *B. abortus* intravenously into a nonpregnant animal and the organisms disappeared in a few hours from the circulation and were present only in the udders and neighboring lymph nodes. They gave an intravenous injection to a virgin heifer 4 years old, and later the bacilli were found in the udders which had never functioned. They examined all the organs of infected animals by guinea-pig inoculation and cultural methods and found *B. abortus* only in the udders or neighboring lymph nodes, and in one instance in the pelvic lymph nodes. They assert, first, that the udders of cows are a common habitat of abortion bacilli; second, that abortion bacilli do not maintain themselves in the bodies of nonpregnant animals elsewhere than in their udders. They, furthermore, experimentally produced the disease by injecting the organisms into the udders, and call attention to the fact that milkers may perpetuate the disease by carrying it on their hands. If other workers prove their claims to be well founded, little wonder can be attached to the presence of *B. abortus* in milk. Previous to those experiments, the same investigators had examined the milk from a number of different dairies. Of 77 samples from 38 dairies, 8 samples from 6 different dairies were infected. In a second series of 140 samples from 4 dairies, Dairy A, 35 samples, showed 11 infected; Dairy B, 33 samples, 7 infected; Dairy C, 34 samples, 2 infected; Dairy D, 38 samples, 2 infected; a total of 214 samples with 30, or 14 per cent., infected.

In another series of 140 cows free from tuberculosis, the milk of nineteen was infected with *B. abortus.* In another series of thirty-six cows with a large proportion tuberculous, the milk of eleven showed *B. abortus.*

Zwick and Krage[4] isolated organisms from the milk of three cows and proved its identity by agglutination tests. They noted no changes in the udders or milk macroscopically, and concluded that *B. abortus* may pass through the udders without causing lesions. They likewise injected strains into the udders of goats and produced the disease in pregnant animals, and further injected them, both by the subcutaneous and intravenous routes, recovering the bacilli in the milk at the end of twenty-four hours, in which they were still present at the end of eight weeks' observation without demonstrable lesions in the udders.

The result of the most comprehensive, purely bacteriologic work

3. Schroeder and Cotton: The Bacillus of Infectious Abortion Found in Milk, U. S. Dept. of Agric. Rep. Bureau of Animal Indust., Circ. 216.

4. Zwick and Krage: Ueber die Ausscheidung von Abortusbacillen mit der Milch infizierter Tiere, Berl. tierärztl. Wchnschr., 1913, **29,** 41.

that has been done on milk was published by Alice C. Evans[5] in 1916. She described three groups of organisms, streptococci, staphylococci and bacilli of the abortus group. A special method of plating was necessary for isolating these bacilli, because a milk containing hundreds of thousands of *B. abortus* might pass unrecognized by the ordinary laboratory method of examination. She studied 192 samples from 161 different cows. In 45, or about 23 per cent., she discovered *B. abortus,* and in 33 of these 45, or 17 per cent. of all the samples, she isolated what she has termed the *B. abortus var. lypolyticus* on account of its fat-splitting character. Two other varieties that she isolated, B and C, resembled cultures obtained from pathogenic sources. Evans also examined by plating, two bottles of certified milk, and found that the *B. abortus* represented 25 per cent. of the total bacteria. This year, 1917, Evans[6] has reported on the further examination of the milk of 23 individual cows and the *B. abortus* developed in 17, or 73.9 per cent. The cultures of 11 samples were studied in detail, and in 9 *B. abortus var. lypolyticus* was found, while in the remaining 2, the bacilli resembled cultures from pathologic material.

The importance of the *B. abortus var. lypolyticus* has not been determined from a pathogenic standpoint.

A. Eichorn and G. M. Potter,[7] referring to them as mutation forms that morphologically and culturally resemble *B. abortus,* say that testing them against pathogenic strains by agglutination and complement fixation failed to give positive reactions. Feeding and inoculation experiments were also inconclusive. One of Evans' most interesting findings is that *B. abortus* from pathogenic sources when grown on mediums containing butter fat for nine and one-half months, has acquired a fat-splitting quality. Eichorn and Potter say that they have had several herds under observation in which abortion occurred occasionally, and in which repeated serologic tests failed to reveal the presence of *B. abortus.* Several questions are suggested to them: (1) Can it be that these fat-splitting organisms play a rôle in such cases, or are they entirely harmless? (2) Are they attenuated forms of the pathogenic variety which have lost some of their characteristics as they acquired the fat-splitting quality? (3) If this is so, may they not under certain circumstances regain their pathogenic properties? (4) Are they detrimental to human health?

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5. Evans, Alice C.: The Bacteria of Milk Freshly Drawn from Normal Udders. Jour. Infect. Dis., 1916, **18,** 437.

6. Evans, Alice C.: The Large Number of Bacterium Abortus var. Lypolyticus Which May Be Found in Milk, Jour. Bact., 1917, **2,** 185.

7. Eichorn, A., and Potter, G. M.: The Present Status of the Abortion Question. Jour. Am. Vet. Med. Assn., December, 1916, **50,** 295.

E. C. Schroeder[8] in 9 series of milk tests, injected 516 samples of milk from 90 dairies into 1,068 guinea-pigs; 103, or about 10 per cent., of the guinea-pigs developed abortus disease and the milk distributed by 29 dairies proved from time to time to be infected with abortion bacilli. He likewise fed guinea-pigs raw, pasteurized and boiled milk, and says that several of the pigs receiving raw milk developed abortion disease.

Ever since 1909, when Holth[9] and Grinstedt,[10] working independently, obtained positive agglutination tests in the serum of cattle infected with abortion disease, serum diagnosis has been generally employed in the determination of this condition. About the same time McFadyean and Stockman[11] showed the presence of antibodies in the blood of infected animals by agglutination tests.

Sven Wall,[12] after 771 examinations, concluded that the agglutination and complement fixation reactions are practical to determine infection if properly carried out. These reactions persist over six months in most animals. He infected a horse intravenously and obtained positive reactions in five days.

Hadley and Beach[13] came to the same conclusion. Brull[14] found these tests very valuable. Zwick and Zeller[15] got positive results in a very large number of cases. Larson[16] in 1912 in this country established that contagious abortion is due to the bacillus of Bang by the complement fixation test. With the exception of the English commission, all workers agree on the value of these tests on the blood

8. Schroeder, E. C.: An Experiment with Raw and Heated Cow's Milk and Its Lesson, with Comments on Bacillus Abortus, Am. Jour. Dis. Child., 1913, **6,** 334.

9. Holth, Halfdan: Die Agglutination und die Komplementbindungsmethode in der Diagnose des seuchenhaften Verwerfens der Kühe. Berl. tierärztl. Wchnschr., 1909, **25,** 686.

10. Grinstedt, P.: The Agglutination Test in the Diagnosis of Contagious Abortion of Cattle, Jour. Compar. Path. and Therap., 1910, **23,** 279.

11. McFadyean, J., and Stockman, Stewart: Epizootic Abortion in Cattle, Report of the Departmental Committee Appointed by the Board of Agriculture and Fisheries to Inquire Into Epizootic Abortion, App. to Part I, London, 1909.

12. Wall, Sven: Ueber die Feststellung des seuchenhaften Abortus beim Rinde durch Agglutination und Komplementbindung, Ztschr. f. Infektionskrankh., 1911, **10,** 23 and 132.

13. Infectious Abortion in Cattle. Jour. Compar. Path. and Therap., 1906, **19,** 191.

14. Brüll, Ziga: Beitrag zur Diagnostik des infektiösen Abortus des Rindes. Berl. tierärztl. Wchnschr., 1911, **27,** 721.

15. Zwick and Zeller: Ueber den infektiösen Abortus des Rindes. Arb. a. d. k. Gsndhtsamte., 1912, **43,** 1.

16. Larson, W. P., and Sedgwick, J. P.: The Complement Fixation Reaction of the Blood of Children and Infants, Using the Bacillus Abortus as Antigen, Am. Jour. Dis. Child., 1913, **6,** 326.

serum of infected animals. Schulz,[17] working in Dresden, in 1912 combined the agglutination test with the intradermal test. His results in the agglutination reactions are identical with those of his predecessors in the work. He found one previous record in the literature of the use of the intradermal test as a diagnostic aid, and he lays great emphasis on its value. He considers as a positive reaction any swelling on the third day of at least 5 mm. diameter. The results, however, vary with the character of the antigen used between 45 per cent. and 100 per cent.

Reinhardt and Gauss,[18] working in 1914 and 1915, report results absolutely in accord with those previously given. They worked in addition, however, with the reactions in the milk serum of infected animals with which Sven Wall had previously worked. Wall found in 25 cows, 23 reacting to blood serum tests. In 11, or about 50 per cent., the milk showed corresponding reactions. Reinhardt and Gauss, examining 27 milk serums, got positive agglutination and complement fixation tests in 21. In 15 cows, when the blood and milk were tested, they got corresponding results in 11.

To determine the time of appearance of antibodies in the blood and milk, Reinhardt and Gauss injected two goats intravenously with a culture of *B. abortus,* the first, half through her pregnancy, and the second, shortly after the birth of two kids. The first goat aborted in seven days. They got positive reactions in the blood and milk of both animals, which lasted longer and with higher dilution in Goat 1 than in Goat 2. No positive reactions were obtained with the blood of the two kids, even though they were with their mother constantly and nursed ten weeks. They conclude that in infected animals antibodies go over into the milk from the blood and last a long time.

Giltner, Cooledge and Huddleston[19] introduced pure cultures of *B. abortus* into the udders of cows and got positive milk serum tests on the following day without any evidence of gross lesions in the udders. They believe that the abortus bacillus has antigenic without pathogenic action. In every case in which *B. abortus* was found by inoculating milk into guinea-pigs, agglutinins were found in the milk, but *B. abortus* was not found in every case that gave positive tests for milk serums. Either the bacilli were present in too small numbers

17. Schulz, W.: Ueber den diagnostischen Wert der Agglutination und der Intrakutanreaktion beim infektiösen Abortus der Kühe, Inaug. Dissert., Dresden, 1912.

18. Reinhardt, R., and Gauss, G.: Untersuchungen über das Vorkommen von Antikörpern gegenüber dem Bacillus abortus infectiosi im Blut und in der Milch abortuskranker Tiere, Ztschr. f. Infektionskr. Haustiere, 1914 and 1915.

19. Giltner, Ward: Contagious Abortion. Rep. Sec. State Board Agric. and Ann. of Exper. Station, Michigan, 1911, p. 155.

to give lesions, or the presence of antibodies in the milk is a passive result from their presence in the blood of the animal.

Investigations bearing on the influence of *B. abortus* on public health have unfortunately been very few.

Mohler and Traum[20] examined the serums of forty-two persons without getting any positive complement fixation or agglutination reactions, although Larson had previously found three positive reactions in 100 serums examined. Out of fifty-six instances in which tonsils and adenoids were inoculated into guinea-pigs by Mohler and Traum, one animal showed the presence of *B. abortus bovinus.*

Larson and Sedgwick,[16] in 1913, assert that after systematically examining the serums of women who had aborted, they found that a larger number gave a positive complement fixation reaction when the *B. abortus* was used as antigen than when the ordinary syphilitic antigen was employed. They had examined, up to that time, the blood of 425 children and found seventy-three, or 17 per cent., positive and 352 negative. They also made agglutination tests which ran parallel. They concluded that the positive reactions were the result of an active immunity due to antibodies generated by the patient, and did not necessarily mean active infection of the individual. In 1915 Larson and Sedgwick[21] further report that it was observed in their original group of 425 children that those receiving milk from an abortus-free herd gave no reaction, while those fed on market milk gave a high percentage. Over 40 per cent. of the children in one institution gave positive reactions, and in one group as high as 48 per cent. reacted. In forty-two new-born children they got no reactions, but one infant in whom artificial feeding was employed on the seventh day, gave a positive reaction on the twenty-first day.

Ramsey[22] examined the blood of fifty-eight boys and an equal number of girls; six boys and one girl gave positive reactions.

Nicoll and Pratt[23] call attention to the fact that several investigators have shown that the ingestion of a large number of bacilli may give antibodies in the blood. The authors had the same results feeding guinea-pigs typhoid bacilli. In testing out a large number of infants and children in the New York Foundling Asylum with agglutination reactions, with very few exceptions they got negative results. One patient in the obstetric ward, having had a miscarriage at the seventh month, gave a positive agglutination reaction of 1 to 300, using

20. Mohler and Traum: Infectious Abortion of Cattle, U. S. Dept. of Agric., Bureau of Animal Indust., Circ. 216, 1911, p. 147.

21. Larson, W. P., and Sedgwick, J. P.: Further Studies on the Epidemic Abortion Reaction in Children, Am. Jour. Dis. Child., 1915, **10,** 197.

22. Am. Jour. Dis. Child., 1915, **10,** 201.

23. Nicoll, M., Jr., and Pratt, J. S.: Does the Bacillus Abortus (Bang) Infect Man? Am. Jour. Dis. Child., 1916, **10,** 203.

B. abortus as an antigen. Two months later her serum still gave a positive reaction 1 to 100. Her infant gave the same reaction. A fosterchild that she was nursing gave a negative reaction. The vaginal discharge, the milk of this mother and the feces of the child were injected into guinea-pigs, with negative results.

Cooledge,[24] in an effort to prove whether or not the *B. abortus* is pathogenic for man, made a number of interesting experiments. He fed 18 guinea-pigs naturally infected milk from 33 to 287 days daily (the milk being tested every four days for antibodies). Two, or 11 per cent., developed antibodies, but no lesions. There occurred 1 abortion and 2 abnormal parturitions. Two controls in noninfected milk, 2 on no milk, remained negative. Two guinea-pigs fed on negative milk, plus cultures, developed antibodies, but no lesions. There is not sufficient evidence from this experiment to warrant the conclusion that infected milk is dangerous to guinea-pigs by ingestion. It has slight antigenic, but no pathogenic, action. Fourteen normal rabbits were fed naturally infected milk for 124 days. Cooledge used 4 controls. Two were fed noninfected milk, 2 no milk. The control gave the same reactions as those receiving infected milk. Only 1 of the 14 gave an increase in antibody content during the 124 days, which persisted 84 days after stopping the feedings. There were no abortions and no postpartum lesions. Six rabbits were fed noninfected milk, plus a culture of *B. abortus;* antibodies developed to a maximum on the forty-second day, weakened on the fifty-second day and were negative in 4 of the 6 on the eighty-fourth day, although the feeding still went on. There were no abortions. The animals had two litters of young, and no postpartum lesions were evident. Infected milk is probably, therefore, not dangerous to rabbits on ingestion. It is not pathogenic, very slightly antigenic. The investigator also fed calves infected milk and got antibodies in the blood, but was not able to say whether they were due to active infection, or active or passive immunity.

Cooledge[25] examined the blood of persons drinking raw milk, pasteurized milk and no milk. Of the 6 drinking raw milk previous to the test, 3 gave positive complement fixation and agglutination tests. Of the 4 persons drinking pasteurized milk, one gave a positive complement fixation test. Those drinking no milk gave negative reactions. He then made a feeding experiment. He gave each of 7 persons 1½ pints daily for 8 weeks of a milk high in *B. abortus* and antibodies. The antibody content of the human serum was determined before

24. Cooledge, L. H.: Is Bacterium Abortus (Bang) Pathogenic for Human Beings? Jour. Med. Research, July, 1916.

25. Cooledge, L. H.: Agglutination Test as a Means of Studying the Presence of the Bacterium Abortus in Milk, Jour. Agric. Research, February, 1916, **5,** 871.

giving the milk, during the consumption, and four weeks after this period. Of the 7, 5 showed an increase in the antibody content, but in no case was this marked. He made another feeding experiment. He gave to 2 adult males daily for six weeks a negative milk, to which was added 10 c.c. of a forty-eight-hour culture of *B. abortus*. No increase in the antibody content was noted, nor were any untoward effects in evidence. Cooledge concludes:

> If the abortus antibodies in the blood were due to an infection of the individual by the organisms being present in the milk, one would expect a fairly high and lasting antibody content; but if the antibodies were due to a passive immunity, one would expect a weak reaction, persisting but a short time after stopping the ingestion of the milk. It is probable, therefore, that the antibodies represent a passive immunity due to absorption from the milk. There is very little evidence that *B. abortus* is either pathogenic or antigenic for human adults at least.

Referring to the reaction present in the blood of young children, Cooledge explains this as perhaps due to the absorption of the antibodies from the milk through the intestinal mucosa as exemplified by the work of Ehrlich and Wassermann, who found young mice capable of assimilating antitoxin through the intestinal tract and developing passive immunity to a certain degree. He does not, therefore, feel that there is sufficient proof to warrant the statement that the *B. abortus* is pathogenic to man.

EXPERIMENTAL DATA

The milk studied in our experiments was obtained from five dairies, called, for convenience, Dairy A, B, C, D and E, over a period of several months, and the number of samples examined with the dates and findings is shown in Table 1.

In order to gather some data as to the prevalence of abortus bacilli in the milk of individual cows, and at the same time to note the possible occurrence of tubercle bacilli in the milk of animals that have reacted to the tuberculin test, which six months previously had failed to react, the milk of nine recent reactors was examined, using the same technic that had been used in examining the mixed milk of the herds. The results are shown in Table 2.

Realizing that we had to deal with a condition which could only be differentiated from tuberculosis in guinea-pigs by most careful examination, a scheme was devised for studying the animals, into which the milk samples were injected, that can be best described by giving a careful history of one of the infected guinea-pigs.

TABLE 1.—DATA CONCERNING MILK SAMPLES STUDIED

Dairy	Test	Date	Guinea-Pig	Result	Percentage Positive
A	1	8/21/16	13	Negative	0
			14	Negative	
			15	Negative	
			16	Negative	
A	2	8/25/16	31	Negative	25
			32	Negative	
			33	Negative	
			34	Typ. Ab. Dis.	
A	3	9/ 2/16	55	Negative	50
			56	Negative	
			57	Typ. Ab. Dis.	
			58	Typ. Ab. Dis.	
A	4	9/23/16	59	Negative	75
			60	Typ. Ab. Dis.	
			61	Typ. Ab. Dis.	
			62	Typ. Ab. Dis.	
A	5	9/26/16	63	Typ. Ab. Dis.	75
			64	Typ. Ab. Dis.	
			65	Typ. Ab. Dis.	
			66	Negative	
A	6	10/ 2/16	71	Typ. Ab. Dis.	75
			72	Typ. Ab. Dis.	
			73	Doubtful	
			74	Typ. Ab. Dis.	
B	7	8/18/16	9	Negative	
			10	Acute Inf.	25
			11	Negative	
			12	Typ. Ab. Dis.	
B	2	8/22/16	19	Typ. Ab. Dis.	
			20	Doubtful	75
			21	Typ. Ab. Dis.	
			22	Typ. Ab. Dis.	
B	3	8/29/16	39	Typ. Ab. Dis.	100
			40	Typ. Ab. Dis.	
			41	Typ. Ab. Dis.	
			42	Typ. Ab. Dis.	
B	4	1/ 5/17	124	Typ. Ab. Dis.	100
			125	Typ. Ab. Dis.	
			126	Typ. Ab. Dis.	
			127	Typ. Ab. Dis.	
C	1	8/15/16	5	Typ. Ab. Dis.	100
			6	Typ. Ab. Dis.	
			7	Typ. Ab. Dis.	
			8	Typ. Ab. Dis.	
C	2	8/31/16	43	Negative	75
			44	Typ. Ab. Dis.	
			45	Typ. Ab. Dis.	
			46	Typ. Ab. Dis.	
C	3	9/13/16	51	Typ. Ab. Dis.	100
			52	Typ. Ab. Dis.	
			53	Typ. Ab. Dis.	
			54	Typ. Ab. Dis.	
C	4	9/28/16	67	Doubtful	75
			68	Typ. Ab. Dis.	
			69	Typ. Ab. Dis.	
			70	Typ. Ab. Dis.	
D	1	8/11/16	1	Typ. Ab. Dis.	100
			2	Typ. Ab. Dis.	
			3	Typ. Ab. Dis.	
			4	Typ. Ab. Dis.	

TABLE 1.—Data Concerning Milk Samples Studied—(*Continued*)

Dairy	Test	Date	Guinea-Pig	Result	Percent. Positive
D	2	8/23/16	23	Typ. Ab. Dis.	100
			24	Typ. Ab. Dis.	
			25	Typ. Ab. Dis.	
			26	Typ. Ab. Dis.	
D	3	8/24/16	27	Negative	75
			28	Typ. Ab. Dis.	
			29	Typ. Ab. Dis.	
			30	Typ. Ab. Dis.	
D	4	8/28/16	35	Typ. Ab. Dis.	100
			36	Typ. Ab. Dis.	
			37	Typ. Ab. Dis.	
			38	Typ. Ab. Dis.	
D	5	1/ 5/17	128	Typ. Ab. Dis.	100
			129	Typ. Ab. Dis.	
			131	Typ. Ab. Dis.	
E	1	1/ 6/17	132	Typ. Ab. Dis.	75
			133	Typ. Ab. Dis.	
			134	Negative	
			135	Typ. Ab. Dis.	
E	2	1/18/17	139	Typ. Ab. Dis.	100
			140	Typ. Ab. Dis.	
			141	Typ. Ab. Dis.	
			142	Typ. Ab. Dis.	
E	3	1/22/17	143	Negative	25
			144	Typ. Ab. Dis.	
			145	Negative	
			146	Negative	

TABLE 2.—Results of Examination of Milk of Cows Reacting to B. Abortus and to Tuberculin—Individual Cows—Tuberculin Reactors

Milk Sample	Guinea-Pig	Necropsy Findings
Dairy C, Cow 1	92	Negative
	93	Negative
	94	Negative
	95	Negative
Dairy C, Cow 2	96	Negative
	97	Negative
	98	Negative
	99	Negative
Dairy C, Cow 3	100	Negative
	101	Negative
	102	Negative
	103	Negative
Dairy C, Cow 4	104	Negative
	105	Negative
	106	Negative
	107	Negative
Dairy C, Cow 5	108	Negative
	109	Negative
	110	Negative
	111	Negative
Dairy C, Cow 6	112	Typ. Ab. Dis.
	113	Negative
	114	Typ. Ab. Dis.
	115	Typ. Ab. Dis.
Dairy C, Cow 7	116	Negative
	117	Negative
	118	Negative
	119	Negative
Dairy C, Cow 8	120	Negative
	121	Negative
	122	Typ. Ab. Dis.
	123	Negative
Dairy F, Cow 9	199	Negative
	200	Negative
	201	Negative

SAMPLE EXPERIMENT

Guinea-Pig 71. Male. Oct. 3, 1915. Weight, 272 gm. Injected intramuscularly into the inner and upper surface of right hind thigh, 5 c.c. of sediment obtained from 800 c.c. of whole milk from Dairy A, suspended in a little saline. Jan. 27, 1917, 116 days after injection, intradermal tests were made, using as antigens abortin, tuberculin, bovine, tuberculin, avian, colin, and typhoidin. Jan. 29, 1917, forty-eight hour readings were as follows:

Colin, N. P.

Abortin, 0; 3.9 by 3.9; marked edema; center yellow; necrosis.

Tuberculin, avian, N. P.

Typhoidin, N. P.

Tuberculin, bovine, 0; 0.6 by 0.6.

Feb. 2, 1917, 122 days after the injection of the milk, the animal was first injected with trypan blue for vital staining, and the dye injections were repeated daily until Feb. 24, 1917. Feb. 16, 1917, 136 days after the milk sediment was injected, the guinea-pig weighed 490 gm., a gain of 218 gm. March 5, the animal was chloroformed, 153 days after the experiment was begun. The following findings were noted:

There is a general adenopathy. The spleen, 5 by 4 cm., is enlarged and hard, contains numerous small nodules. The liver contains a few nodules. The kidneys and lungs are negative. There is an abscess in the right testicle with a firm wall. The left testicle is small and atrophic.

Bone lesions: The left ninth rib is the seat of a tumor mass, the size of a large pea, containing deep blue cheesy matter surrounded by a dense layer of tissue. The right ninth and tenth ribs are the seats of small tumors, the size of a grain. The left seventh rib at the point of insertion to the vertebra has a tumor the size of a small pea, containing cheesy matter. Spleen culture on potato glycerin serum agar, positive in eight days.

Agglutination Tests: Blood taken from the heart of the guinea-pig before chloroforming, March 15, 153 days after the milk injection, gave a positive reaction in a dilution of 1 to 1,000 to 1 to 4,000.

Recapitulating, the procedure was briefly as follows: Several weeks after the milk had been injected, intradermal tests were made, using various antigens; at this time blood was taken from the heart for agglutination determinations. Some animals were then repeatedly injected with a vital stain, following which they were chloroformed. The various organs were studied macroscopically as far as the vital staining permitted, and microscopically, and in most cases an effort was made to isolate the invading organism. The results have been carefully tabulated in a manner shown in Table 3 and the more minute details, referring particularly to cutaneous hypersensitiveness, agglutination reactions, gross and microscopic lesions and cultural characteristics of the invading organisms, will be reported in later communications.

Studying the results in detail leads to some interesting observations. Of the twenty-two samples of milk obtained from the mixed herds of five different dairies, twenty-one, or over 95 per cent., showed definite *B. abortus* infection. None showed the presence of tubercle bacilli in sufficient number to cause tuberculosis in guinea-pigs. *The*

milk of Dairy A, from which the one sample was obtained that produced no lesions, infected 50 per cent. of the animals that were injected, the experiments extending over three months. *The milk of Dairy B* infected about 80 per cent. of the animals injected, the experiments extending over a period of six months. *The milk of Dairy C* infected about 88 per cent. of the animals injected, the tests extending over a period of two months. *The milk of Dairy D* infected 95 per cent. of the animals injected, the experiments extending over a period of six months. *The milk of Dairy E* infected 66 per cent. of the animals injected, the tests having been made with only a short interval between them.

It is interesting to note that Dairy A, from which the one negative sample was obtained, was evidently a less seriously infected herd, or harbored a less virulent type of organism, than the other dairies, because in no single experiment were 100 per cent. of the guinea-pigs infected. The importance, in this connection, of using large quantities of milk and a sufficient number of animals cannot be overestimated. The quantity used, 800 c.c., is much larger than is usually recommended in the literature, and this unquestionably accounts for the large percentage of positive results. Furthermore, if fewer animals had been used in the individual tests, the results would not have been nearly as striking. In several instances the first two or three guinea-pigs were apparently uninfected, while the last animals examined were overwhelmed with the disease, showing in guinea-pigs, as in cattle, the marked individual susceptibility to the abortus bacillus.

A study of the results obtained by injecting the milk of individual cows reacting to the tuberculin test, which had not reacted to it six months before, shows that none of these animals was excreting tubercle bacilli in sufficient quantity in their milk to infect guinea-pigs with tuberculosis. About 22 per cent. of them were harboring pathogenic *B. abortus,* which corresponds fairly well with previous observations where the milk of individual cows was tested in this connection. The number tested, however, was too small to draw positive conclusions, but the result is at least suggestive.

At this point it may be well to discuss a little more in detail the methods that were used to establish a correct diagnosis in each animal, and briefly to summarize the results. The agglutination test was made according to the usual technic. Reactions under 1 to 100 were not considered positive. In the serum of the infected animals the reaction was positive in dilutions of from 1 to 600 to 1 to 1,000, and sometimes in dilutions greater than 1 to 2,000. The complement fixation test was not made because most investigators are of the opinion that the agglutination test is quite as reliable and its technic is much more simple.

The intradermal tests were always positive in infected animals, the

characteristics of the reaction being marked induration, frequently with central necrosis, an areola at least 1 cm. in diameter, with persistency of the reaction over the forty-eighth hour. The organisms were isolated in over 20 per cent. of the infected animals. In the remaining animals, either no attempt was made to isolate the organisms, or, on account of the special vital staining dye that had been injected, the bacilli did not grow on the mediums incidental to conditions the exact nature of which is being studied. By reinoculation of the spleen or isolated organisms from infected animals, the identical disease was produced in guinea-pigs. The isolated organisms were further identified by an abortus serum produced by a known *B. abortus* strain. It is of profoundest interest to note that where animals had been mated for months, infection in either the male or female practically always resulted in a failure of impregnation.

The pathologic lesions, both macroscopic, which have been referred to earlier in this paper, and microscopic will be further studied and reported in a later communication. The disease attacks principally the lymph nodes, spleen and sex organs, with a special selective action toward the last, but it may also manifest itself in the liver, bones, lungs, eyes and kidneys in some cases.

CONCLUSIONS

As far as can be concluded in a preliminary report from a limited amount of material, it may be said:

1. *B. abortus* is, for practical purposes, always present in the certified milk produced in the San Francisco Bay regions.
2. Tubercle bacilli are not present in this same milk in sufficient number to give tuberculosis to guinea-pigs, although this conclusion may prove incorrect on further experimentation.
3. If the above conclusion is correct, there is no necessity for pasteurizing certified milk on account of any danger that it may possess as a disseminator of bovine tuberculosis to infants.
4. It is not unlikely that in many previous milk tests for tubercle bacilli, the anatomic lesions of bovine abortion disease in the guinea-pig were mistaken for tuberculosis.
5. If the *B. abortus* is present in certified milk to the extent evident from these experiments, it is difficult to consider it pathogenic for infants, without, so far as is known, ever having produced recognizable lesions on post mortem examination.
6. The result of this work, however, is one more definite indication that it is of greatest importance to study the abortus problem from every angle to be absolutely certain of its bearing on the health of infants.

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TABLE 3.—Results of Intradermal Injections of Milk Sediment in Guinea-Pigs

Guinea-Pig	Sex	Weight, Gm.	How and When Injected	Time Interval, Days	Cutaneous Hypersensitiveness				Agglutination	Necropsy Findings	Cultural Results	End Weight, Gm.	Remarks
					B. Abortus Broth, 1-2	B. Abortus Protein 1-1,000	B. Typhosus Protein 1-1,000	Tuberculin bovine, glycerin 1-2 human; Alc. Precip. 1-3					
126	M	294	Milk from Dairy B, 1/5/17	54	2.8 by 2.8 M. I. R.	1.4 by 1.4	N. P.	....	1-200 1-1,000	General lymphadenitis; spleen 3.5 by 2; scarred, nodular; testes atrophic; other organs negative.	Spleen cultures positive in 5 days	480	4/7/17, trypan blue injections begun 4/24/17, chloroformed
128	M	382	Milk from Dairy C, 1/5/17	54	3.1 by 3.4	1.6 by 1.6	N. P.	....	1-2,000	General lymphadenitis; spleen 3.5 by 2; nodular, enclosed in inflammatory tissue from mesentery; testes atrophic; other organs negative.	Spleen cultures positive	470	3/5/17, injection of dianil blue 3/26/17, chloroformed

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THE PHENOLSULPHONEPHTHALEIN ELIMINATION IN INFANTS AND YOUNG CHILDREN *

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Since the original publication, in 1910, by Rowntree and Geraghty[1] of the results of their experimental work with phenolsulphonephthalein in determining the functional capacity of the kidney, the value of the test has received such ample confirmation as to establish it among the essentials for careful diagnosis in renal diseases.

It may be desirable to recapitulate briefly its rationale and practical limitations. No attempt has been made to cover all the literature on observations on adults, but all of Rowntree and Geraghty's publications have been consulted and enough of the more recent articles to see that their opinions are, in the main, corroborated by others.

Phenolsulphonephthalein is an ideal substance for the study of renal function, being practically nontoxic and nonirritating, readily absorbed and rapidly eliminated through the kidneys. Even the strongest advocates of indigocarmin, its nearest rival, admit the superiority of phthalein for studying the total function of both kidneys. Owing to its avidity as an acid and the production of a pure red color in alkaline solution, it lends itself readily to accurate colorimetric estimations.

From the study of a variety of experimental renal lesions in the dog, Eisenbrey[2] concludes that the phenolsulphonephthalein test is one of the most satisfactory, and, at the same time, most delicate methods of estimating the functional activity of the kidney.

Although the phenolsulphonephthalein which circulates in the blood after injection presents the same concentrations in the liver, pancreas and salivary glands as it does in the kidney, Rowntree and Geraghty[3] have shown that only a small amount of the drug appears in the bile and none in the pancreatic juice or saliva. It is clear, they believe, "that the capacity for picking out the molecules of phthalein from the infinitely dilute solution in the blood and passing them on into the

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1. Rowntree, L. G., and Geraghty, J. T.: Jour. Pharm. and Exper. Therap., 1909-1910, **1**, 579.

2. Eisenbrey, A. B.: Jour. Exper. Med., 1911, **14**, 366.

3. Rowntree, L. G., and Geraghty, J. T.: Arch. Int. Med., 1912, **9**, 284.

urinary secretion in comparatively concentrated solution, is a function specific to the kidney."

They have also obtained fairly conclusive proof that the cells of the tubules play the most important rôle in the excretion of phthalein, and that a much smaller amount must also be eliminated through the glomeruli. Furthermore, none of the usual diuretics in therapeutic doses have any appreciable effect in hastening or increasing the elimination, although, under experimental conditions, those diuretics in large doses which are believed to exert a stimulating effect on the secreting cells of the tubules, slightly increase the phthalein output.

Both from experimental and practical evidence, Geraghty and Rowntree[4] have found the intramuscular injection of a solution of phenolsulphonephthalein to be the method of choice. Elimination begins (in normal adults) in from five to eleven minutes; from 40 to 60 per cent. of the phthalein injected appears in the urine by the end of the first hour, and from 60 to 85 per cent. at the end of the second hour. Elimination is practically complete in the two hours, as only a trace appears in the third and fourth hours.

After intravenous injection, the drug appears in from three to five minutes, and from 63 to 80 per cent. is eliminated within the first hour. Subcutaneous injections result in such large variations as to vitiate their value.

In no disease, other than renal, has any very marked and consistent reduction of phthalein excretion been noted. Experimentally, Rowntree and Geraghty[3] have found a distinct reduction in very severe anemias. Straub and Bancroft (quoted by Rowntree and Geraghty[3]) have shown that in such conditions, experimentally studied, the tubular function of the kidneys may be entirely removed. This would indicate, again, that the tubules chiefly are concerned in the excretion of phthalein, but that the glomeruli are capable of excreting some of the drug. In secondary anemia, in the absence of nephritis, the output of phthalein has been found to be almost normal.

Acute Nephritis.—In acute nephritis, the capacity of the kidney to excrete can readily be determined by the phthalein test, but this means little prognostically, on account of the rapidity with which variations occur. Rowntree[5] has encountered patients who excreted only 10 per cent. of phthalein in two hours during an acute attack of nephritis, with a rise to 24 per cent. four days later. In two weeks the output had become normal. Frequent repetitions of the test, therefore, are essential for prognosis. He has never met with any instances of

4. Geraghty, J. T., and Rowntree, L. G.: Jour. Am. Med. Assn., 1916, **62**, 811.
5. Rowntree, L. G.: Am. Jour. Med. Sc., 1914, **147**, 352.

"increased permeability" in acute nephritis. Thayer and Snowden[6] note considerable reduction in the phthalein output in some instances of the cloudy swelling of the kidneys which accompanies acute infections.

Chronic Nephritis.—So far as prognosis in chronic nephritis is concerned, when the phthalein excretion is only moderately reduced, the immediate outlook is favorable, but tests should be applied intermittently to determine whether the case is stationary or progressive. The possibibty of an acute exacerbation becoming superimposed on the chronic process, necessitates caution in giving an opinion (Rowntree[5]). In general, it may be said that advanced nephritis always shows a decreased output. Thayer and Snowden[6] assert that in not a single instance of severe chronic nephritis studied within the last five years have they met with a good phthalein elimination.

On the other hand, instances of a normal output occasionally are encountered in patients with undoubted chronic nephritis. Such occurrences have been reported by Pepper and Austin,[7] and Baetjer.[8] These authors suggest that a hyperpermeability of the kidney for phthalein may exist. Thayer and Snowden consider that these cases are more or less characteristic in their clinical manifestations and are often roughly classed as chronic parenchymatous nephritis. Their most striking clinical features are the elective impermeability of the kidney to salt and the resulting tendency to hydrops. With regard to most of the other tests of function, the kidneys appear to react normally and, except for the dropsy, there may be few disturbing symptoms. As Rowntree[5] points out, the phthalein test at least furnished correct information so far as immediate prognosis in these cases of hyperpermeability is concerned, as they did not have a fatal termination while under observation. In the earlier stages of chronic parenchymatous nephritis, and in mild cases, Rowntree and Geraghty[3] find little disturbance of function, but where there is a marked decrease in phthalein elimination, marked renal changes must be present. In the presence of only traces of phthalein in the urine, or when it is entirely absent, they consider that the prognosis is grave, even though no signs of uremia exist.

In clear-cut instances of chronic interstitial nephritis, however, they find the test most valuable. Almost all such cases show more or less diminution in phthalein excretion. In all but one of twenty-two patients of this type, Brown and Cummings[9] found a parallelism between the phthalein output and the clinical symptoms.

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6. Thayer, W. S., and Snowden, R. R.: Am. Jour. Med. Sc., 1914, **148,** 781.
7. Pepper, O. H. P., and Austin, J. H.: Am. Jour. Med. Sc., 1913, **145,** 254.
8. Baetjer, W. A.: Arch. Int. Med., 1913, **11,** 593
9. Brown, Phillip King, and Cummings, W. Taylor: Jour. Am. Med. Assn., 1916, **66,** 793.

According to Rowntree,[5] it has been shown experimentally that a moderate degree of passive congestion shows a normal phthalein output, which decreases as the congestion becomes more marked, but returns to normal with the earliest signs of improvement in the circulation. Clinical confirmation of this theory is found in cardiorenal cases. Patients with moderately advanced nephritis associated with a moderate myocardial insufficiency often exhibit a fair renal capacity. An increase in the phthalein output may be the first evidence of a restoration of cardiac compensation, and hence indicates a favorable immediate prognosis. A low excretory capacity with marked increase in blood urea or total nonprotein nitrogen, indicates that the kidneys are seriously affected, or that the heart is in an extremely precarious condition. With or without "cumulative phenomena," a low excretory capacity persisting after there is clinical evidence of cardiac improvement, indicates severe nephritis and an unfavorable prognosis.

Uremia.—In eleven of sixteen patients with uremia, who died during the attack, Rowntree and Geraghty[3] found the phthalein elimination to be absent, or only a trace.

Austin and Eisenbrey[10] note that a marked decrease in elimination occurs synchronously, as a rule, with the onset of symptoms of intoxication (vomiting). Therefore, they conclude that the phthalein test would seem to be a better indication of the ability of the kidney to eliminate the toxic substances responsible for the symptoms of renal insufficiency than are the anatomic changes or the elimination of total nitrogen or chlorids.

In twenty-one cases coming to necropsy, Rowntree and Geraghty[3] found a remarkable uniformity between the phthalein output and the pathologic findings. In one patient with polycystic kidneys who died of pneumonia, the output had been normal. This corroborates the known fact that polycystic kidneys usually are found at necropsy quite unexpectedly.

In summing up the value of the phthalein test, Rowntree, Marshall and Baetjer[11] expressly stipulate that whenever the output of phthalein is decreased even but slightly, the total nonprotein nitrogen, or the blood urea, or both, should be determined. In other words, reliance cannot be placed on the phthalein test alone in the study of nephritis, no matter how valuable may be its corroborative evidence.

Comparatively few investigations in the phthalein eliminations in infants and children have been made. In 1912, before the Section on

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10. Austin, J. H., and Eisenbrey, A. B.: Jour. Exper. Med., 1911, **14,** 366.
11. Rowntree, L. G., Marshall, E. K., Jr., and Baetjer, W. A.: Arch. Int. Med., 1915, **15,** 543.

Diseases of Children, R. M. Smith[12] reported a small series, as follows: Five patients with normal kidneys show from 32 to 52 per cent. elimination in one hour. The ages of the patients were not given. Fifteen patients with acute nephritis, varying in age from 3½ to 7 years, eliminated from 28 to 61 per cent. (average 44 per cent.) within one hour, and six patients with pyelitis showed an output of from 20 to 60 per cent. (average 37 per cent.) for one hour. Most of these cases of acute nephritis seem to have been mild, none proving fatal. Edema was present in nine of the fifteen. The lowest figures, 28 and 30 per cent., were found, as a rule, in the worst cases. The highest figure, 61 per cent., was found in a patient in whom the duration of the disease was not given, and who therefore may have belonged to the category of chronic parenchymatous nephritis. Another possible chronic case showed only 30 per cent. at two different tests. It must be remembered that all these figures are for one hour's excretion only, using 3 mg. of phthalein instead of 6 mm. Smith considers that the phthalein test shows the ability of the kidney to eliminate toxins and whether there is danger of uremia. It does not assist in determining the ability of the kidney to eliminate protein, salts and water.

In connection with a study of the nonprotein nitrogen and urea of the blood, Tileston and Comfort[13] estimated the phthalein output in several groups of patients varying in age from 6 months to 11 years. Only six of the patients were under 2 years of age. In five healthy children from 3 to 9 years of age, the phthalein output in two hours varied from 78 to 81 per cent. In three children with acute nephritis, from 2½ to 9 years of age, two of whom also suffered from pneumonia and scarlatina, respectively, the output varied from 39 to 54 per cent. in two hours. The figures for the remainder may be tabulated.

Disease	No. of Cases	Age	Percentage of Phthalein in 2 Hrs.
Lobar pneumonia	7	8 mos. to 9 years	45 to 85
Lobar pneumonia (Urine contained granular casts and albumin)	1	15 mos.	17
Scarlatina	8	17 mos. to 11 yrs.	49 to 86
Typhoid fever	6	3 to 10 yrs.	57 to 75
Tuberculous meningitis	2	18 mos. and 10 yrs.	79 and 55
Cerebrospinal meningitis	1	4 yrs.	78
Mixed group, pertussis, diphtheria, chorea, etc.	12	2½ to 10 yrs.	30 to 86

The authors conclude that the phthalein test is very valuable in the diagnosis of nephritis, showing probably better than any one other

12. Smith, Richard M.: Am. Jour. Dis. Child., 1913, **5**, 25.
13. Tileston, W., and Comfort, C. W.: Am. Jour. Dis. Child., 1915, **10**, 278.

method the degree of impairment of renal function. In the diagnosis of uremia and as a guide to diet, it is inferior to blood analysis, because a low phthalein output may occur without retention of nitrogen. They are also inclined to believe that the child's kidney has a better excreting capacity than that of the adult.

Leopold and Bernhard[14] also studied the nonprotein nitrogen of the blood and the phthalein output in sixty-five children.

In a group of fifty hospital patients, from 2 to 14 years of age, suffering from a variety of diseases, but free from any evidences of nephritis, the figures for phthalein excretion in two hours varied from 50 to 96, the average being 70 per cent.

The figures for the group of cases of nephritis were as follows:

Acute nephritis, 5 cases.........	23	60	69	74	85
Chronic nephritis, 5 cases.......	19	33	44	64	73
Passive renal congestion........	38	40	42	58	78

They conclude that so far as their own cases are concerned, the figures in the nonnephritic groups are practically identical with figures obtained in adults, and that the changes in the subjects of renal disease correspond to the changes observed in adults.

Fishbein,[15] from a study of a small group of children and adults, concludes that there seems to be a general lowering of the renal function during the latter stages of scarlet fever. In nearly all uncomplicated cases in which examination was made from the third to the fifth week, a total phthalein output averaging 55 per cent. was observed, as compared with the usual figures of from 65 to 85 per cent.

Hempelmann,[16] in a study of the phthalein elimination in seven patients with orthostatic albuminuria, from 8 to 12 years of age, found an average decrease of 12.9 per cent. in the phthalein output with the patients in the position of accentuated lordosis during the test, compared with the results after a night in bed. Two normal patients showed 70 and 83 per cent. before and 71.5 and 81.8 per cent. after being in the lordotic position.

Barker and Smith[17] found normal phthalein elimination in all but one of six young male patients, from 16 to 25 years of age, suffering from orthostatic albuminuria. In three that were tested before and after standing erect for two hours, there was a slight reduction in elimination, but not enough to be of great significance.

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14. Leopold, J. S., and Bernhard, A.: Am. Jour. Dis. Child., **11,** 432.
15. Fishbein, M.: Jour. Am. Med. Assn., 1913, **61,** 1369.
16. Hempelmann, T. C.: Am. Jour. Dis. Child., 1915, **10,** 418.
17. Barker, L. F., and Smith, F. J.: Am. Jour. Med. Sc., 1916, **41,** 44.

Our own studies in phthalein elimination were made on seventy-five patients in the wards of the Children's Hospital of Philadelphia, in the services of one of us (J. C. G.) and of Dr. J. P. Crozer Griffith and Dr. Alfred Hand, Jr. We take this opportunity for acknowledging our indebtedness to them.

Patients with definite renal disease were studied whenever they presented. With this exception no attempt was made at selection other than to pick out males and thus facilitate the collection of urine. The ages of the patients varied from 3 weeks to 10 years. Forty-four were under 1 year of age; seven were from 1 to 2 years, and twenty-four from 2 to 10 years. The technic was as follows:

Technic.—The older children passed urine before the test, but the infants and younger children were not catheterized at this time. The repetition of catheterization of these infants did not seem warranted. At this age, urination occurs so frequently that the amount of urine residual at the time the test was begun must have been small, in the absence of any signs of distention of the bladder. It also seems to us that the percentage of error due to residual urine in nonobstructive cases must at all times be very small. This error must be that due to the different color of the residual urine and an equal amount of distilled water, when used as a diluent, for the phthalein contained in 1,000 c.c. of the final solution (500 c.c. in our cases). The infants and younger children were held on Bradford frames, and under all the patients were placed clean, dry, cotton pads. If any urine was found to have been spilled on the pad during the test, the results were discarded. In the case of all the patients who could not voluntarily hold the urine, the penis was securely fastened in the mouth of a urinal and 0.5 c.c. of a solution containing 3 mg. of phenolsulphonephthalein (half the amount used in adults) was injected deeply into the lumbar muscles.

Catheterization with a soft rubber catheter was performed at the end of 70 minutes, or 130 minutes, or both, except in some of the older children who were able to void. The time was extended 10 minutes over the one and two hour periods to allow for the interval required for the phthalein to appear in the urine after intramuscular injection, and thus make the results comparable with those obtained after intravenous injection.

In view of the almost universal use of the intramuscular route, except in the presence of some local condition such as marked edema which would interfere, we believe it would be more desirable to allow exactly one or two hours after intramuscular injection and thus make these the standard readings. When intravenous injections are used, we would have different figures for the standard.

At the end of the time allowed, the urine passed, and that obtained by catheter was alkalinized with a solution of sodium hydroxid; diluted to 500 c.c. with water, instead of 1,000 c.c. (to correspond to the reduction in the amount of the drug used); and the amount of phthalein estimated by comparison with the Dunning colorimeter. Cloudy urine was filtered before making the reading, and if the results were at all doubtful, the diluted urine was mixed with equal parts of water, another reading made and the result of the reading doubled. The Dunning colorimeter was used, partly because a Duboscq colorimeter was not available at the hospital, but chiefly because of its low cost and greater practicability for the use of the general practitioner. The results by this method are admitted to be reasonably accurate.

We regret that so many of the estimations were made only at the end of the

first hour. At the beginning of the study, we had decided to use the one-hour period only. Later, we utilized the two-hour period in the younger infants, catheterizing only once. The earlier results for one hour are included, however, as they may be compared with other results for the same period of time.

The cases are grouped in Table 1 as follows: Group I, Acute Infections; II, Miscellaneous Diseases; III, Acute and Chronic Nephritis; IV, Cardiorenal Disease; V, Pyelitis.

In preparing a summary of the results in the various groups, we found no noteworthy difference in the phthalein elimination of patients with albumin and casts in the urine — apart from the true nephritic groups — and of those whose urinary findings were negative.

While absolute accuracy demands catheterization at the end of both the first and second hour periods, it is admitted that voluntary urination in the nonobstructive types of genito-urinary diseases gives results which are quite accurate. In a comparison of percentages found in our catheterized and uncatheterized patients, the differences were negligible.

Table 2 gives the condensed results for the two-hour periods; Table 3 for one-hour, and Table 4 for total results. In Table 5 all cases are grouped according to their ages, except those with nephritis, and Nos. 1 and 27 (Table 1, Group II).

In the groups of acute infections, miscellaneous diseases and pyelitis (Table 1, Groups I, II and V) no marked diminution in the amount of phthalein eliminated was noted, except in two of the three patients suffering from tuberculous meningitis. One of these (No. 1) died on the same day that the test was made, and the low phthalein elimination (15 per cent. in two hours) was of no clinical significance. The second patient (No. 27) gave less than 5 per cent. of phthalein in two hours, but lived for seven days. The presence of large amounts of albumin and an excessive number of leuckocytes in the urine suggests the possibility of tuberculous lesions in the kidneys, which would account for their poor function. Neither of these cases is included in any of the summaries. The cases of nephritis (Table 1, Groups III and IV) showed a distinct diminution in phthalein percentages, as would be expected. Presumably all of them belonged to the type of parenchymatous nephritis. None died under observation except the patient with cardiorenal disease (No. 57, Group IV), whose death was cardiac and not uremic.

The case of pernicious anemia (No. 38, Table 1, Group II) showed an output of 62.5 per cent. for two hours, although the red cells fell as low as 200,000 in one of the counts made previous to the test. Death did not occur until fifty-seven days after the test.

TABLE 1.—Phenolsulphonephthalein Elimination in Various Groups

Group I, Acute Infections

No.	Age	Sex	Diagnosis	Day of Disease	Remarks	Result	Urine, Albumin	Microscopic Examination	Phthalein Test 1 Hr.	Phthalein Test 2 Hr.	Phthalein Test Total
2	9 mos.	♂	Acute bronchitis	5	Temperature 98-101	Recovered	2 neg. 2 tr.	4 negative	50	20-25	70-75
21	9 yrs.	♂	Acute bronchitis	5	Afebrile; voided	Recovered	3 neg.	3 negative	50-55	20	70-75
24	10½ mos.	♂	Acute bronchitis	18	Temp. 98.4-100	Recovered	3 neg.	3 negative	60	10-15	70-75
25	13 mos.	♂	Acute bronchitis	6	Temp. 100	Improved	1 neg. 2 tr.	1 hyaline and cylindroids +; 3 leuko. +	50	15	65
30	4 yrs	♂	Acute bronchitis	?	Temp. 98.2-100; voided	Recovered	3 neg.	3 negative except few cal. ox. cryst.	45	20	65
63	5½ yrs.	♂	Acute bronchitis	5	Temp. 98-99.4	Recovered	1 tr.	1 few hyaline	45	—	—
12	6 mos.	♂	Acute bronchitis	14	Afebrile 3 days	Recovered	3 neg.	3 negative	45	15	60
35	6 yrs.	♂	Acute bronchitis	20	Afebrile 7 days	Recovered	3 neg.	3 negative	55	25	80
26	9 mos.	♂	Bronchopneumonia	9	Temp. 99.2	Died 17 days after	2 +	2 cylindroids; leuko. +++	45-50	20	65-70
45	6½ mos.	♂	Bronchopneumonia	15	Afebrile for 3 days	Recovered	2 tr.	2 gran. cast ++	30	25	55
52	5 yrs.	♂	Lobar pneumonia	7?	Afebrile for 4 days; voided	Recovered	2 tr.	2 cylindroids; 1 leuk. ++	35	25	60
39	6 yrs.	♂	Lobar pneumonia	25	Afebrile for 10 days; von Pirquet +; voided	Recovered	1 tr. 1 neg.	1 few hyaline and dark gran. casts; 1 neg.	70	10-15	80-85
20	1 yr.	♂	Acute otitis media	9	Temp. 99.4	Recovered	3 neg.	3 negative	35	5-10	40-45
50	6 mos	♂	Ac. otitis media and retropharyngeal absc.	?	Temp. 100.3	Recovered	2 tr.	2 negative	30	—	—
32	8 yrs	♂	Typhoid fever	21?	Afebrile 2 days; voided	Recovered	2 neg. 1 tr.	3 negative	60	10	70
33	7 yrs.	♂	Typhoid fever	40	Afebrile several days; voided	Recovered	3 neg.	2 negative; 1 few gran. casts	—	70	70
1	4 yrs.	♂	Tb. meningitis	35	Very poor condition	Died in few hours	1 tr.	1 leuko. +++	0	15	15
22	19 mos.	♂	Tb. meningitis	8	Very poor condition	Died 3 days later	1 tr.	1 leuko. ++	60	15	75
27	3½ mos.	♂	Tb. meningitis	?	Very poor condition	Died 7 days later	3 ++	3 leuko. ++++	0	5	5

GROUP II, MISCELLANEOUS DISEASES

60	10 mos.	♂	Chronic bronchitis	27	....	Improved	2 neg. 1 tr.	3 negative	—	75	75
47	4 yrs.	♂	Catarrhal jaundice	12	....	Recovered	2 neg. 1 tr.	2 negative; 1 leuko. ++	30	20	50
9	18 mos.	♂	Tb. pleurisy	30	von Pirquet +	Improved	1 ft. tr.	1 negative	45	—	—
3	10 mos.	♂	Hydrocephalus	300	von Pirquet +	Unimproved	6 neg.	6 negative	—	65	65
29	17 mos	♂	Infantile atrophy	90	Poor condition	Unimproved	2 neg. 1 tr.	2 neg.; 1 few gran. casts	50	—	—
54	7 mos	♂	Infantile atrophy	180	Poor condition	Improved	3 neg.	2 neg.; 1 few gran. casts	—	80	80
7	7 mos.	♂	Infantile atrophy	33	Poor condition	Improved	3 neg. 1 tr.	4 negative	60	—	—
10	3 mos.	♂	Infantile atrophy	45	Fair condition	Recovered	2 neg.	2 negative	60	10	70
13	2 mos.	♂	Infantile atrophy	?	Fair condition	Recovered	3 neg.	3 negative	40	—	—
15	4 mos.	♂	Infantile atrophy	54	Good condition	Recovered	3 neg.	3 negative	55	—	—
17	3 mos.	♂	Infantile atrophy	90	Poor condition	Recovered	3 neg.	3 negative	65	—	—
18	5 wks.	♂	Infantile atrophy	35	Poor condition; received breast milk	Recovered	4 neg.	4 negative	45	—	—
36	3 mos.	♂	Infantile atrophy	?	Poor condition	Died in 6 days	3 neg.	3 negative	—	70	70
41	4 mos.	♂	Infantile atrophy	120	Poor condition	Unimproved	1 neg.	1 negative	35	5	40
64	8 mos.	♂	Infantile atrophy	60	Fair condition	Recovered	3 neg.	3 negative	45	—	—
67	3 mos.	♂	Infantile atrophy	60	Fair condition	Recovered	3 neg.	3 negative	55	—	—
73	2 mos.	♂	Infantile atrophy	60	Poor condition; fed on breast milk	Recovered	3 neg.	3 negative	35	—	—
72	2 mos.	♂	Infantile atrophy	60	Poor condition	Recovered	2 neg. 1 tr.	2 neg.; 1 few hyaline and gran. casts; leuko. ++	20-25	—	—
44	3 mos.	♂	Infantile atrophy	22	Poor condition	Died 28 days later	3 tr.	2 hyaline and granular casts +; 1 leuko. ++	30	—	—
5	4 mos.	♂	Infantile atrophy	68	Fair condition	Recovered	4 neg.	4 negative	—	60	60
74	7 mos.	♂	Infantile atrophy	Since birth	Poor condition	Improved	1 neg.	1 negative	50	—	—
75	7 mos.	♂	Infantile atrophy	Since birth	Poor condition	Improved	1 neg.	1 negative	60	20	80
40	5½ mos.	♂	Chr. enteritis, gonorrheal epididymo-orchitis	35	Fair condition	Recovered	2 neg. 2 tr.	1 few gran.; 3 negative	50	10-15	60-65
4	5 mos.	♂	Chronic enteritis	40	Good condition	Recovered	4 neg.	4 negative	—	60	60
19	5 mos.	♂	Chronic enteritis	35	Good condition	Recovered	3 neg.	3 negative	—	70	70
61	6½ mos.	♂	Chronic enteritis	30	Fair condition; Temp. 99-100	Recovered	3 neg.	2 neg.; 1 gran. casts +	45	—	—

TABLE 1.—PHENOLSULPHONEPHTHALEIN ELIMINATION IN VARIOUS GROUPS—(*Continued*)

GROUP II—(*Continued*)

No.	Age	Sex	Diagnosis	Day of Disease	Remarks	Result	Urine, Albumin	Microscopic Examination	Phthalein Test 1 Hr.	Phthalein Test 2 Hr.	Phthalein Test Total
55	13 mos.	♂	Chronic enteritis	30	Fair condition; Temp. 98–102; von Pirquet +	Improved	2 neg.	2 negative	40	—	—
43	5 mos.	♂	Acute enteritis	7	Poor condition Temp. 98–103	Improved	5 neg. 4 tr.	6 neg.; 2 few hyl. casts; 1 few gran. casts	50	15	65
34	10 mos.	♂	Indigestion	14	Fair condition	Recovered	1 neg. 1 tr.	2 negative	—	80	80
8	3 mos	♂	Indigestion	15	Good condition; von Pirquet ++	Improved	3 neg.	3 negative	50	20	70
11	3 wks.	♂	Indigestion, edema	9	Good condition; fed breast milk	Recovered	3 neg. 1 tr.	4 negative	—	60	60
14	4½ mos.	♂	Indigestion	49	Very good condition	Recovered	3 neg.	3 negative	55	—	—
23	6 yrs.	♂	Indigestion	?	Poor condition; von Pirquet + voided	Improved	3 neg. 4 tr	7 negative	25	35	60
46	3½ mos.	♂	Indigestion	40	Good condition	Recovered	3 neg.	3 negative	60	—	—
53	10 mos.	♂	Indigestion	29	Good condition	Recovered	2 neg.	2 negative	35	—	—
70	3 mos.	♂	Indigestion	18	Good condition	Recovered	3 neg.	3 negative	60	—	—
28	5 mos.	♂	Indigestion	16	Fair condition	Recovered	2 neg.	2 negative	45-50	25	70-75
31	2 yrs	♂	Indigestion	12	Fair condition	Recovered	7 neg.	7 negative	—	80	80
71	3 mos.	♂	Indigestion	40	Fair condition	Recovered	3 neg.	3 negative	60-65	15	75-80
61	14 mos.	♂	Congenital lues	Since birth	Fair condition; 2 Wass. +	Improved	5 tr.	2 negative; 3 leuko. ++	65	—	—
66	7 mos.	♂	Hydrocephalus	Since birth	....	Unimproved	4 neg.	4 negative	35	—	—
38	3 yrs.	♂	Pernicious anemia	70	Voided; poor condition; Temp. 98-101	Died 57 days later	9 neg. 1 tr.	9 neg.; 1 few gran. casts	45	15-20	60-65
56	4½ yrs.	♂	Intestinal parasites	?	Good condition Temp. 99–100	Recovered	6 neg. 2 tr.	8 negative	35	30	65

GROUP III, NEPHRITIS

No.	Age	Sex	Diagnosis	Day of Disease	Remarks	Average Daily Amount Urine, Ounces	Urine,	Microscopic Examination	Phthalein Test 1 Hr.	Phthalein Test 2 Hr.	Phthalein Test Total
6	7 yrs.	♂	Chronic nephritis	?	Syst. B. P. 120; diast. 68; no edema; seen 3 mos. later; still had alb. and casts	38	13 +	13 few hyl. and lt. gran. casts	50	15	65
42	10 yrs.	♂	Chronic nephritis 1 yr. after scarlatina	365	Syst. 112-108; diast. 90-82; no edema; had alb. and casts before adm.; voided	38 (19-43)	6 neg.	5 neg.; 1 few hyl. and dark gran. casts	30-35	15	45-50
62	9 yrs.	♀	Chronic nephritis; sinus arrhythmia	64	Syst. 136; diast. 88; slight edema, legs and eyelids; Temp. 99-100; voided	22	3 neg. 3 +	5 hyl., gran., waxy and epithelial casts +; 1 neg.	40	10-15	50-55
68	4 yrs.	♀	Acute nephritis	21	Syst. 110; diast. 70; marked edema; Temp. 99-100	6½ to 10½	18 +	18 hyl., gran. and blood casts +	3/7/17 — 3/19/17 10	3/7/17 30-35 3/19/17 15	30-35 25
65	3 yrs.	♂	Acute nephritis	15	No edema; Temp. 99.8-100	28	10 ++ to +++	10 gran. casts ++; blood casts +; leuko. +++	35	5	40
51	9 yrs.	♀	Acute nephritis	38	Syst. 210; diast. 187(?); slight edema eyelids; died 7 days later; voided	24	15 ++ to +++	15 hyl. and gran. casts +; leuko. +++	20	15	35
37	5 yrs	♂	Acute nephritis	16	Syst. 82-92; diast. 60-64; no edema; toxic; had suprsn. urine at first; recovered; voided	20 to 22	8 tr.	8 hyl. and gran. casts +	11/11/16 25 11/14/16 50	11/11/16 20 11/14/16 15-20	45 65-70
48	7 yrs.	♂	Acute nephritis	38	Syst. 105; diast. 55; moderate edema legs Temp. 98-100	36	11 tr.	11 hyl. and gran. casts +	40	10	50

GROUP IV, CARDIORENAL

No.	Age	Sex	Diagnosis	Day of Disease	Remarks	Average Daily Amount Urine, Ounces	Urine,	Microscopic Examination	Phthalein Test 1 Hr.	Phthalein Test 2 Hr.	Phthalein Test Total
57	6½ yrs	♀	Chronic endocarditis; chronic nephritis	365	Syst. 130; diast. 80; marked edema; Temp. 97-102; salt-free diet; voided; died 6 weeks later	22	10 +++	10 hyl. and gran. casts ++	15	25	40

TABLE 1.—PHENOLSULPHONEPHTHALEIN ELIMINATION IN VARIOUS GROUPS—(*Continued*)

GROUP V, PYELITIS

No.	Age	Sex	Diagnosis	Day of Disease	Remarks	Result	Urine, Albumin	Microscopic Examination	Phthalein Test		
									1 Hr.	2 Hr.	Total
16	6 mos.	♂	Pyelitis	27	No alb. or casts for 2 wks. before test	Recovered	3 neg. 10 tr.	Pus cells, 15-20 to high power field uncentrifuged urine; hyl. casts occas.	30	15-20	45-50
49	4 yrs	♀	Pyelitis	42	....	Improved	39 ++ to +++	Pus cells ++ to +++; 4 few hyl. casts; 1 few gran. casts	40	25	65
58	9 mos	♂	Pyelitis	40	....	Recovered	2 neg. 14 tr.	Pus cells ++ to +++	45	—	—
69	11 mos.	♂	Pyelitis	?	Temp. 100-103	Recovered	13 tr.	Pus cells 3 to 28 to high power field uncentrifuged	60	—	—

TABLE 2.—Condensed Results for Two-Hour Periods

Groups	Number of Cases	Average Percentage of Phthalein Eliminated			Extremes		
		1 Hr.	2 Hrs.	Total	1 Hr.	2 Hrs.	Total
I and V	16	47.8	18	65.8	30–70	7.5–25	42.5–82.5
II	12	45.8	18.8	64.6	25–62.5	5 -30	40 -80
III and IV	9	31.75	15	46.75	10–50	5 -25	25 -67.5

Table 2 emphasizes the fact that there was no noteworthy difference between the results obtained in the acute infections and in the miscellaneous diseases. There is, therefore, no further object in separating them. In general, the proportion of phthalein eliminated in the first and second hours corresponds to that found in adults; nor was there any ascertainable reason for the occasional discrepancies of a large output in the second hour, such as was found in Cases 45 and 52, although in Case 57 the marked edema may have been the cause of delayed elimination. As the maintenance of the normal proportion in the first hour is not essential, while the total result for two hours is generally accepted for a standard interpretation, we would advocate the estimation of only the total amount of phthalein eliminated in two hours in children who require catheterization, thereby avoiding the necessity for repeating it.

TABLE 3.—Results for One-Hour Periods

Groups	Number of Cases	Average Percentage of Phthalein Eliminated in the First Hour	Extremes
I, II and V	53	46.9	22.5–70

This table includes a number of patient on whom only a 1-hour observation was made. The results very closely approximate those in Table 2.

TABLE 4.—Total Results

Groups	Number of Cases	Average Percentage of Phthalein Eliminated in Two Hours	Extremes
I, II and V	39	66	40–82.5

This table includes the patients on whom only one observation was made at the end of two hours. Again, the results closely approximate those in Table 2.

TABLE 5.—Grouped According to Ages, Etc.

GROUPS I, II AND V

Age	Period	No. Cases	Per Cent.	Per Cent.
Under 3 months	1-hour	11	47.7	(22.5–65.0)
	2-hour	5	69.4	(60.0–77.5)
3 to 6 months	1-hour	11	44.3	(30.0–60.0)
	2-hour	11	61.4	(40.0–80.0)
6 to 12 months	1-hour	13	48.6	(35.0–60.0)
	2-hour	8	69.4	(42.5–80.0)
1 to 2 years	1-hour	6	51.6	(40.0–65.0)
	2-hour	3	73.0	(65.0–80.0)
Over 2 years	1-hour	12	44.8	(25.0–75.0)
	2-hour	12	66.9	(50:0–82.5)

From a study of Table 5 it is clear that the ages of the patients had no influence on the elimination of phthalein. Even Patients 11 and 18 (Table 1) aged 3 and 5 weeks, showed an output of 60 per cent. for two hours and 45 per cent. for one hour, respectively.

CONCLUSIONS

1. The observation is confirmed that the elimination of phenolsulphonephthalein is not markedly decreased in any disease other than renal.

2. Even the youngest infants and children show about the same capacity for phthalein elimination as do adults.

3. Preliminary catheterization in the absence of retention of urine is unnecessary.

4. For purposes of comparison, a uniform technic should be adopted and maintained.

5. We believe that in children a single collection exactly two hours after the injection into the lumbar muscles of 6 mg. of phthalein, should be the method of choice. The necessity for continuous or repeated catheterization thereby would be avoided.

6. An entirely different standard must be used for the accelerated output resulting from intravenous injections. The latter need only be employed when local conditions, such as marked edema, prevent the use of the intramuscular route.

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THE USE OF PANCREATIC VITAMIN IN CASES OF MARASMUS *

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INTRODUCTORY

Vitamin was first isolated from rice polishings in 1911 by Casimir Funk and shown by him to be the agent which prevented beriberi. It was also in this year that Mendel and Osborne did their comprehensive work on the feeding of single purified proteins to white rats. In the latter work it was established that in addition to nutrients the diet of a growing rat demanded the presence of certain substances hitherto unknown, and which these workers found present in protein-free milk and in centrifuged butter fat. Funk had meanwhile not only extended his isolation of vitamin to other substances than rice polishings — among them yeast — but had shown that aside from the effect on polyneuritic conditions the vitamin was an essential factor in growth stimulation. From these beginnings the development of the importance of vitamin as a growth factor has been rapid. Of all the studies, those of E. V. McCollum of Wisconsin, and his co-workers, perhaps deserve most attention. McCollum has summed up the dietary factor as follows: In addition to a suitable nutrient content, a growing animal demands in his diet:

1. The presence of a "fat-soluble A" (his name for Mendel's butter fat factor).

2. The presence of a "water-soluble B" (his name for Funk's vitamin).

3. The absence of any toxic factors.

Experiments have shown that whatever the composition of vitamin, it is probably not a simple amin. The nomenclature problem would be easier to settle if the substance had been satisfactorily identified chemically. Unfortunately, all attempts to purify it or to isolate it in an approximately pure form have resulted in failure and in loss of power on the part of the vitamin-containing factor. This result has given rise to certain controversies and hypotheses that tend to confuse the general student of the subject. Funk, for example, claims that Mendel's butter fat does not contain a new type of vitamin, but is merely contaminated with the water-soluble vitamin he has described.

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McCollum, on the contrary, is thoroughly convinced that there are at least two types of growth-producing substances, and has suggested dropping the name vitamin altogether and substituting the names given above as temporary descriptive terms pending the settlement of the problem of chemical structure. Hess has shown that however much scurvy may resemble beriberi, the yeast vitamin that curbs the latter does not control the former disease, and furthermore, that the orange juice that cures scurvy is not a growth stimulant, and in that sense at least is not a vitamin.

Still another difficulty in the study of vitamins lies in the lack of any chemical test for their presence. At present, we have only two ways of determining this, namely, by producing polyneuritic conditions in pigeons through the feeding of polished rice and then treating the birds with the vitamin-containing substance, or by feeding rats on a maintenance diet and then by the addition of the vitamin to the diet noting the upward tendency of the growth curve as a result. These tests require careful control and involve many factors. Even now we do not know whether the antineuritic vitamin is identical with the growth-producing vitamin, whether there is a group of chemical substances with similar properties, or particular substances with specific function. If the latter is true, then orange juice contains a vitamin that is specific for scurvy. If, on the other hand, vitamins are substances which combine the power of growth stimulation with antineuritic properties, then orange juice contains no true vitamin at all.

In spite of all this confusion incident to the status of the problem today, the study is making progress. A marked addition to the practical possibilities of the subject was developed when Seidell established the feasibility of obtaining active vitamin from its crude solution by means of a special form of fuller's earth. This form, known as Lloyd's reagent, has the power, when shaken with a crude vitamin extract, of adsorbing the vitamin. Apparently, no loss of activity occurs in the vitamin in the process, no appreciable amount of contaminative substance is removed from the solution by the reagent, and the result is the possibility of an activated agent whose bulk is composed of an inert, harmless-to-man material, and which has the properties of a pure (?) vitamin as far as effects go.

PANCREATIC VITAMIN

In a previous communication, Eddy has confirmed the efficiency of this means of separation for the removal of pancreatic vitamin from its aqueous solution. In the feeding experiment about to be described the Lloyd powder, activated by an aqueous solution of pancreatic vitamin, was used. The steps in the preparation may be briefly summarized as follows:

Pancreatic glands of lambs were obtained within twenty-four hours of their removal and minced in a meat chopper. These minced glands were thoroughly extracted with 95 per cent. alcohol to which had been added enough hydrochloric acid to make it approximately 0.8 per cent. acid. The acid-alcohol extract was filtered and the filtrate evaporated to dryness before the fan at 25 C. The residue was thoroughly extracted with water and the water extract filtered and concentrated before the electric fan to such a volume as to make 1 c.c. correspond to 2.7 gm. of pancreas. This was an arbitrary unit selected as a means of standardizing subsequent preparations. One c.c. of this extract contained 0.0075 gm. of nitrogen. To a liter of this water extract was then added 50 gm. of Lloyd's reagent and the mixture made thorough by shaking in a mechanical shaker for thirty minutes. This mixture was left to stand over night and at the end of that time the sediment was filtered off with a suction funnel, dried before the fan, repowdered in a mortar, and finally dried to constant weight in a vacuum desiccator over sulphuric acid. This dried powder was found by experiments on rats to have the vitamin effect, and the tests with the filtrate indicated that the removal of the vitamin was quantitative. Furthermore, no amino-acids were separated from the solution by the powder. While the amount of nitrogen in the powder varies somewhat with the preparation, it is usually about 0.03 + gm. nitrogen per gram of powder.

The advantages of this powder for dosage are obvious. In the first place, the powder itself is entirely harmless to the animal, being inert except for its adsorbing power. Second, it enables one to give a relatively heavy dose of vitamin without using a large bulk, as 1 gm. of the powder contains the vitamin of 54 gm. of pancreas. Third, the vitamin effect is not modified by the presence of other factors.

Having demonstrated the efficiency of this vitamin preparation in growth stimulation with white rats, it seemed desirable to try its effect in cases of infant malnutrition and especially in cases of marasmus. Up to the present, ten cases have been studied, of which six were cases of marasmus. Nine of these patients were treated in the wards of the New York Hospital. One was treated under our direction at the Babies' Hospital, the case being supplied through the kindness of Dr. F. H. Bartlett.

While the number of cases at present reported is small, the results are suggestive, and are reported here more for stimulation of collateral investigation than because of the conclusiveness of the evidence. As presented, the cases are classified in three groups. Each group will be discussed in detail, and it will suffice here to indicate merely the basis of classification.

Group I: In this group is covered the case of a single patient, John G., a typical marasmic, whose growth stimulation was apparently induced by vitamin while being fed a carefully controlled, practically vitamin-free diet of cereal, orange juice and condensed milk. This case was further controlled by a study of five rats fed on a diet identical with that of the baby and with the vitamin content varied to meet experimental needs.

Group II: In this group are placed five patients, including three

with marasmus, who at the time of beginning the vitamin treatment were declining in weight and whose weight curves were deflected upward without other apparent means than by the addition of vitamin.

Group III: In this group are placed four patients who had begun to gain on the diet supplied, and to whose diet the vitamin was added in the hope of stimulating better growth. These cases add little definite evidence as to the stimulation by vitamin. They show that the addition of the vitamin was followed by growth, but whether this was due to the vitamin or not cannot be demonstrated by the evidence. In some cases the rate of growth was apparently increased.

EXPERIMENTAL

Group I: Patient John G.

The patient was 6 months old on admission to the hospital; weight on admission, 7 pounds 9 ounces; a typical marasmic in appearance.

History.—The chief complaint was continued loss of weight, and the admission diagnosis was malnutrition. Father and mother well; one other child, 2 years old; one miscarriage. This baby was a full term normal child, of normal birth; weight at birth was said to have been 12 pounds; nursed one month; then fed two-thirds water, one-third grade "A" milk; 8 ounces every two hours, and one feeding at night. After a few weeks the infant began vomiting and had green stools, no mucus or curds; five or six movements per day. The baby was sent to a hospital and after three weeks was sent to the country, from which it returned apparently healthy. Then it began to lose weight again, and was being fed at this time 30 ounces boiled water, 3 ounces barley water, 20 ounces grade "A" milk, with two lumps of sugar; 5 ounces every three hours; often the infant refused part of a feeding.

Physical Examination.—Emaciated, facies of an old person; bones prominent; no craniotabes; eyes and ears normal; no rigidity of neck; no pulsations; chest long and slender; ribs prominent; lungs and heart-beat normal.

DISCUSSION

On admission to the hospital, Oct. 9, 1916, the patient was given an observation period of twenty-two days, during which several varieties of diet were tried. During this time the patient's weight varied greatly, as shown by Chart 1, and the net change was a loss of 2 ounces. October 31, the patient weighed 7 pounds 8 ounces, and during the six days preceding this date had declined in weight some 12 ounces (see chart). During the first eighty days the character of the diet was a combination of condensed milk in various strengths, with cereals and a daily allotment of orange juice. To this diet was added at two different periods a dosage of pancreatic vitamin. The dose consisted of 2 gm. of Lloyd's reagent activated by vitamin, 1 gm. being given with a feeding of cereal twice a day. Analysis showed that 1 gm. of this activated vitamin powder contains 0.03 gm. of nitrogen. There is also reason to believe that this indicates a dosage

of not more than 0.12 gm. of vitamin per day. In the accompanying chart (Chart 1) have been indicated the patient's weight curve, the calorie value of the food actually consumed per day, the vitamin periods and various incidents bearing on the progress, such as abscesses, coughs, etc., together with a record of the number of daily stools. Beginning about the seventieth day the patient was gradually transferred from the condensed milk to a whole milk formula. The results of the treatment can therefore be best studied from the chart.

It will suffice, then, to call attention to certain features bearing on the results. For example, it will be noted that from the twenty-first to the twenty-ninth day the addition of the vitamin was accompanied by a marked rise in weight of 8 ounces, though the food consumption was the lowest in the feeding period. On the twenty-ninth day the feedings were increased to gratify the appetite, coincident with the rise in the weight curve, and the net gain in this first vitamin period was 21 ounces in twenty-one days. On the forty-third day the vitamin was discontinued. This change was made to determine whether the growth would continue after the vitamin had been removed from the diet. As has been previously found to hold with rats, the effects of the ingested vitamin apparently continued five days, the patient gaining 6 ounces during this period. During the next four days there was no gain, though the food intake remained the same, 563 calories. Since that number of calories was sufficient to provide growth for a 9-pound boy, and since it bore out the other result, the observations on rats, it seemed to indicate the stimulating power of the vitamin and the failure of growth when vitamin was removed from a diet poor in natural vitamin. At this time the patient was markedly improved in appearance, face oval from tissue formation instead of pinched and wan, bones of the legs well covered and every indication of normal tissue growth. Without changing the diet otherwise, vitamin feedings were resumed on the fifty-third day. The second administration period was for twenty-three days, with a net gain in weight of 8 ounces. At the end of this period the vitamin treatment was stopped and the patient gradually introduced to a whole milk diet. The results indicated that the power to utilize vitamins in such a diet had been acquired and the child has since gone on to complete recovery. He was discharged from the hospital on the one hundred and thirty-eighth day after admission, and at that time weighed 13 pounds, a net gain of 5 pounds 6 ounces since admission.

CONTROL EXPERIMENTS WITH RATS

Five rats were selected and a daily diet of cereal and condensed milk was fed them. Each rat received and completely consumed each day 2 ounces of condensed milk. They received each day as much

cereal of the kind given John G. as they would eat, and the amount consumed was noted by weighing back each day. None of the rats received orange juice. In this respect only did they differ from John G. in the character of their diet. Three of the rats were fed this diet alone and weighed each day. As a result, two of the rats developed

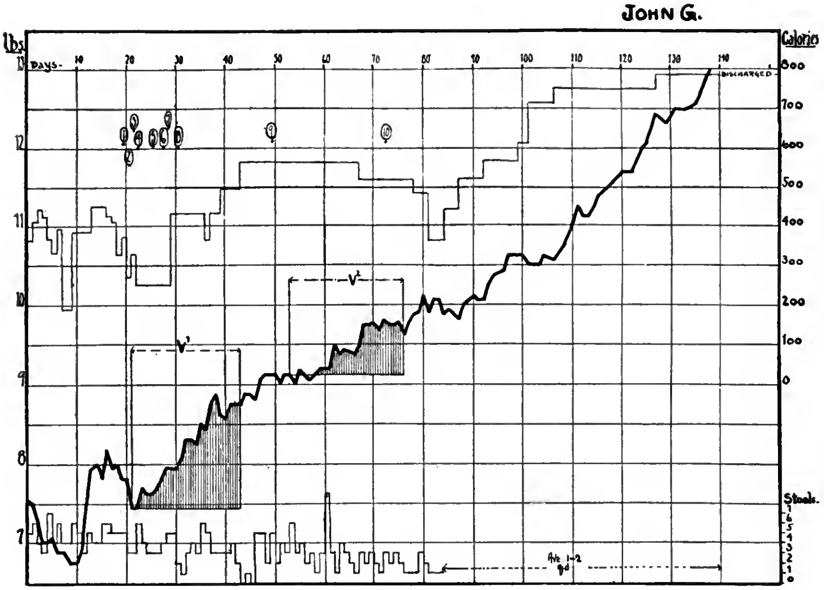

Chart 1.—Group I, No. 1.

Chart 1.—1. On the twentieth day the patient developed a cough. 2. On the twenty-first day the cereal was reduced from three times a day to twice a day. The patient cried during the night. 3. On the twenty-second day the stools showed free starch. 4. On the twenty-third day an anal abscess was opened. The stools continued to show free starch until the twenty-fifth day. 5. On the twenty-fifth day the stools showed soluble starch but no free starch. 6. On the twenty-seventh day the appetite was good and there was no starch. 7. From the twenty-eighth to the forty-third day no starch was observed in the stools. 8. On the thirty-first day the patient developed a cough. 9. From the forty-ninth day to the time of discharge three tablespoonsful of orange juice were given daily. 10. On the seventy-third day the patient developed a bronchitis and mustard paste was applied every four hours up to the eighty-fourth day.

V^1 = From the twenty-first day to the forty-third day the patient received each day 2 gm. of Lloyd powder, activated with pancreatic vitamin. The powder was administered by mixing 1 gm. with each cereal feeding. The result was 20 ounces gain in twenty-two days, a normal growth.

V^2 = After a period of ten days without vitamin, during which the patient settled down to a level growth curve, the treatment described under V^1 was resumed. This was continued from the fifty-third to the seventy-sixth day. The result was the resumption of growth but at a slower rate; 8 ounces were gained in twenty-three days. During the latter part of the period the patient developed a bronchitis. At the end of this period the patient was placed on a whole milk formula. From that time to the time of discharge the patient grew normally.

scurvy and died at the end of twenty-three and twenty-four days, respectively. The remaining one of these three did not develop scurvy. Two of the five rats were given the above diet plus 1 gm. of the activated Lloyd powder (mixed with the cereal) each day. These rats developed no signs of scurvy, but as this was also true of one of the other group, we cannot be sure that this vitamin is antiscorbutic. Experiments are under way to determine this point. The effect of the introduction and removal of vitamin from the diets of these five control rats is shown in Chart 2. The figures are as shown in Table 1.

TABLE 1.—Effect of Vitamin on Rats Fed John G.'s Diet

	Two Rats Fed on Condensed Milk, Cereal and 1 Gm. Vitamin Powder per Day		Three Rats Fed on Condensed Milk, Cereal and No Vitamin		
	Rat 20	Rat 22	Rat 16	Rat 17	Rat 18
Weight November 8, gm.	68	48	78	66	76
Weight at end of period, gm.	88	73	62 (dead)	67 (dead)	76 (alive)
Days elapsed	13	13	24	23	24
Net gain or loss, gm.	+20	+25	—16	+1	±0
Total cereal eaten, gm.	446	452	768	695	825
Average daily consumption, gm.	34	35	32	30	34

Average daily condensed milk was 2 ounces per day per rat.

The results in this table show clearly two things, namely, that the cereal and condensed milk diet is markedly lacking in natural vitamins, and that the addition of pancreatic vitamin to such a diet is sufficient to convert it into an efficient growth-producing diet. In order to check this matter further, Rats 20 and 22 were deprived of the vitamin for the next twelve days. As in the case of the child, the stimulation of the ingested vitamin apparently continues for some time after stopping its feeding. The results are shown on the chart and in Table 2.

TABLE 2.—Effect of Stopping the Vitamin in Rats 20 and 21

	Rat 20	Rat 22
Weight November 21, gm.	88	73
Weight December 3, gm.	88	86
Net gain or loss, gm.	±0	+13
Days elapsed	12	12

During this period the rats were fed on cereal and condensed milk but without any vitamin.

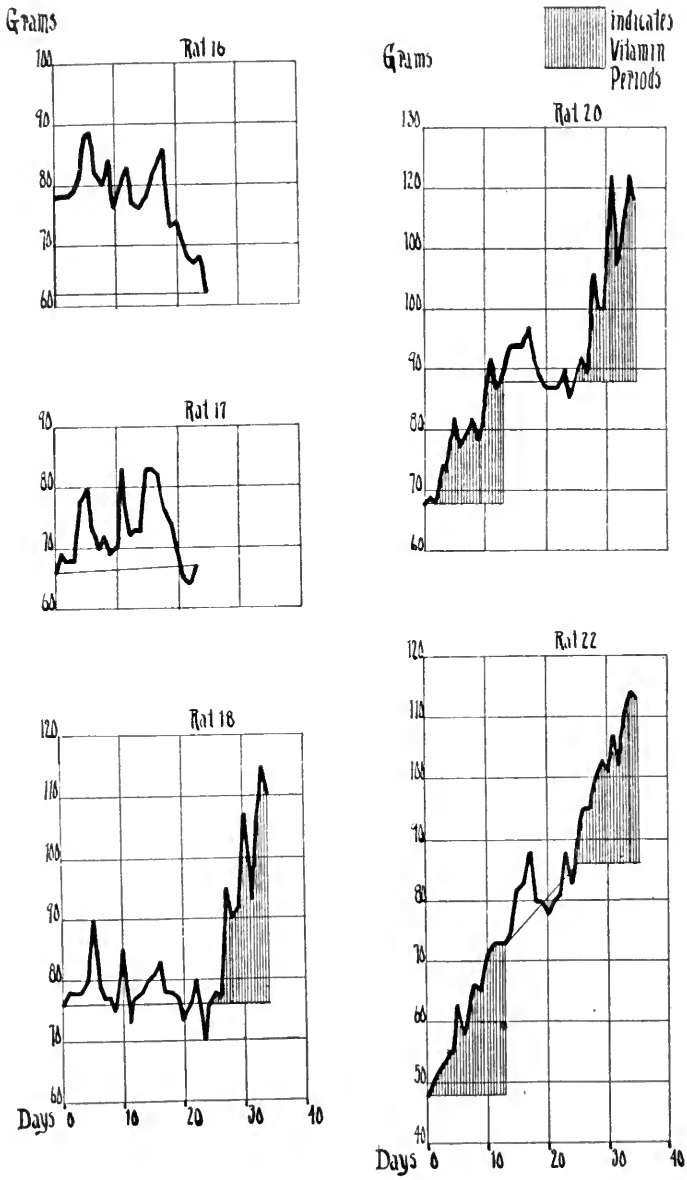

Chart 2.—Group I, No. 2. Rats fed on John G.'s diet with and without vitamin.

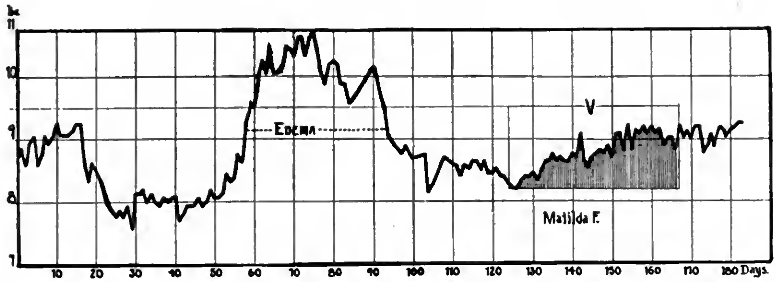

Chart 3.—Group II, No. 1.

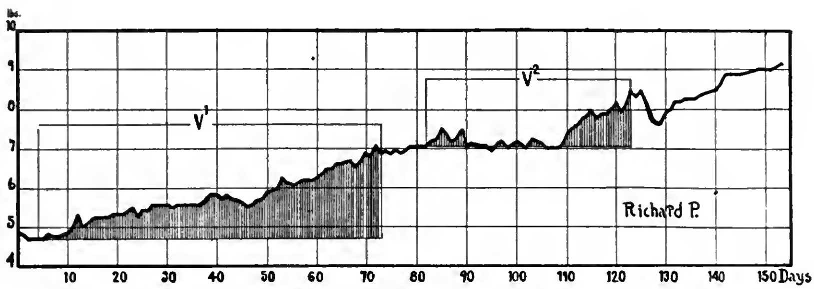

Chart 4.—Group II, No. 2.

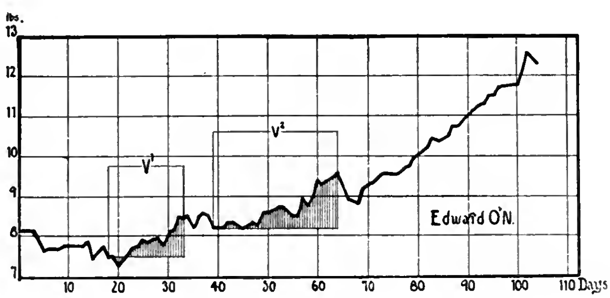

Chart 5.—Group II, No. 3.

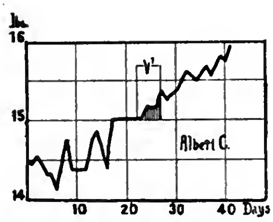

Chart 6.—Group II, No. 4.

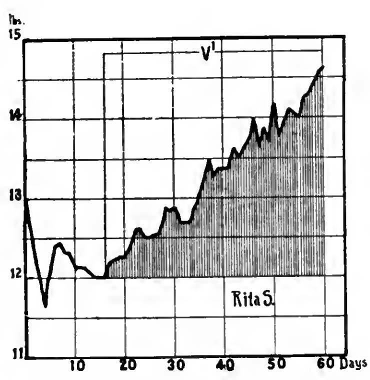

Chart 7.—Group II, No. 5.

Still further to determine the effect of the vitamin on this diet, Rats 20, 22 and 18 were then fed as before, but with the vitamin added for a period of ten days. The marked rise in this period seemed to justify the conclusions reached from the preceding data (Chart 2).

TABLE 3.—Effect of Resuming Vitamin After a Period Without It

	Rats 20, 22, and 18 Were Fed for a Period of Ten Days on Cereal and Condensed Milk, the Addition of 1 gm. of Vitamin Powder per Day Following a Nonvitamin Period		
	Rat 20	Rat 22	Rat 18
Weight December 3, gm.	88	86	76
Weight December 14, gm.	118	113	111
Net gain, gm.	+30	+27	+35
Days elapsed	10	10	10

CONCLUSIONS

From the combined results with the patient and the rats the evidence seems to warrant the following conclusions:

1. A diet of condensed milk and cereal is markedly deficient in natural vitamins.

2. The addition of pancreatic vitamins to such a diet influences the growth of both rats and child.

3. The dosage employed in the case of John G. was sufficient to produce growth of a normal rate, though not to the extent noted in the rats.

4. The treatment produced no harmful effects of any sort.

Group II: Patients: Matilda F., Richard P., Edward O'N., Albert C. and Rita S.

These five children had suffered loss of weight or failure to grow on the diets supplied. These diets presented considerable variety, but all the patients were either declining in weight or static at the time the vitamin was administered, and in all cases this administration was followed by growth without other change in the diet. The diet in no case was increased until growth had begun, and demands for more food became necessary on this account.

Two of these children were too small to take cereal when the treatment was begun (Richard and Edward). These infants received their first dosage in the form of the aqueous extract, 10 c.c. being added to a bottle of milk, twice a day. When these children became able to eat cereal they received the activated powder also. To the other three

the vitamin was given as in the case of John G. — 1 gm. activated powder mixed with a feeding of cereal twice a day.

In the case of Matilda F. (Babies' Hospital case) the child received her first impulse toward normal growth after 123 days of experimentation with other diets. The five charts of Group II (Charts 3, 4, 5, 6 and 7) show the results of the treatment graphically; the figured weight gains are shown in Table 4.

TABLE 4.—(CHARTS 3 TO 7) WEIGHT GAINS IN GROUP II

	Matilda F.	Richard P.	Edward O'N.	Albert C.	Rita
Ounces gained or lost in previtamin period	—9	—2	—10	+8	—16
Number days elapsed	124	4	18	22	16
Rate of gain or loss	—0.07*	—0.5*	—0.55*	+0.36*	—1
Ounces gained in first vitamin period	+16	+30	+15	+6	+42
Number days elapsed	43	69	15	6	44
Rate of gain	+0.37*	+0.43*	+1.0*	+1.0*	+0.95*
Ounces gained or lost in first postvitamin period	+1	+4	—4	+9	
Number days elapsed	16	9	6	14	
Rate of gain or loss	+0.06*	+0.44*	—0.66*	+0.64*	
Ounces gained in second vitamin period	....	+24	+23		
Number days elapsed	....	41	25		
Rate of gain	....	+0.58*	+0.92*		
Ounces gained in second postvitamin period	....	+10	+42		
Number days elapsed	....	31	40		
Rate of gain	....	+0.32*	+1.05*		

* Rate determined by dividing total gain or loss in ounces by number of days elapsed.

All of these patients have now fully recovered, and sufficient time has elapsed to indicate permanent recovery.

These cases seemed to offer further evidence for the conclusion that pancreatic vitamin in the dosage and form given offers a medium through which growth may be stimulated in this type of patient. In the cases of Edward and Richard the evidence was especially strong. In both a cessation of the vitamin resulted in a lowered rate, and the restoration to a higher rate was obtained by resuming the vitamin without other change in the diet. These two cases also demonstrate another feature of the treatment, namely, that the use of vitamin ultimately results in the development of the power to use the natural vitamins in the food, for when these babies were put on a whole milk diet after a second period of vitamin they were able to grow on it.

At the beginning of the experiment they could not utilize such a diet for growth. By stopping the vitamin treatment and noting whether this power has developed, one has a check on the duration of the treatment.

In all these five cases the babies gave every indication of marked improvement physically. They were all discharged as cured and sufficient time has elapsed to feel certain of the permanence of the recovery.

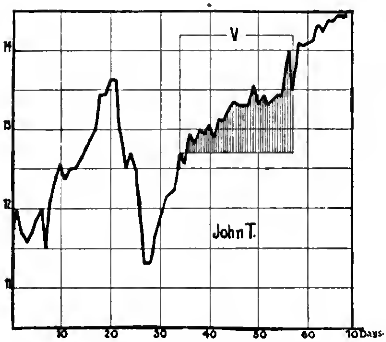

Chart 8.—Group III, No. 1.

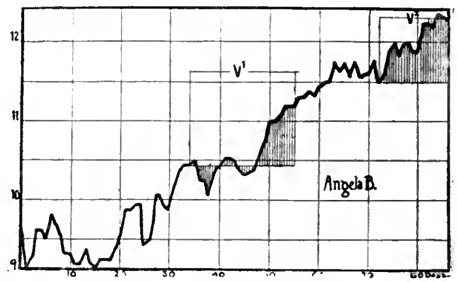

Chart 9.—Group III, No. 2.

Group III: Patients: Arthur J., Elizabeth C., Angela B. and John T.

These four children had suffered from malnutrition and had been tried on various diets. At the time the vitamin was begun they had already started to grow on a diet consisting of a whole milk formula

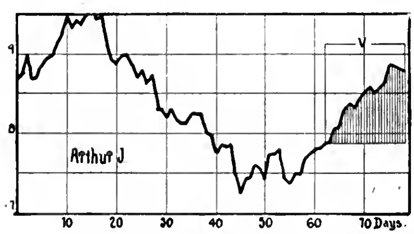

Chart 10.—Group III, No. 3.

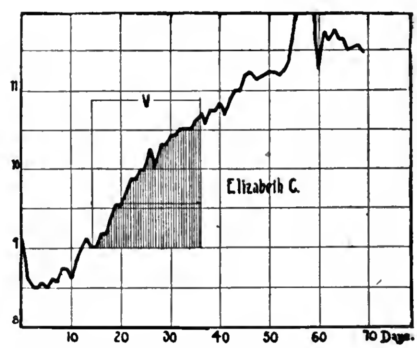

Chart 11.—Group III, No. 4.

and cereal. Vitamin was added to this diet to see if it would increase the effect of the natural vitamin in the milk. The graphs are shown in the four charts of Group III (Charts 8, 9, 10 and 11). The figures showing the gain or loss will be found in Table 5.

TABLE 5.—(CHARTS 8 TO 11) SHOWING GAIN OR LOSS IN GROUP III

	John T.	Angela B.	Arthur J.	Elizabeth C.
Ounces gained or lost in previtamin period	+15	+23	—13	—2
Number days elapsed	34	34	62	14
Rate of gain or loss	+0.44*	+0.68*	—0.2*	—0.14*
Ounces gained in first vitamin period	+13	+12	+15	+27
Number days elapsed	23	21	17	22
Rate of gain or loss	+0.56*	+0.54*	+0.88*	+1.22*
Ounces gained or lost in postvitamin period	+17	+5	....	+13
Number days elapsed	12	17	....	33
Rate of gain	+1.41*	+0.29*	....	+0.39*
Ounces gained in second vitamin period	....	+12		
Number days elapsed	....	14		
Rate of gain	....	+0.85*		

The cases in Group III are not offered as positive evidence. At best they seem to indicate that the addition of vitamin to the diet may have increased the growth rate in certain of the cases, but from the fact that growth had already begun, this effect cannot be demonstrated to be due to the vitamin. They are included in order to present a complete picture of the entire experiment. At least they do not contradict the evidence of Groups I and II.

SUMMARY

The use of pancreatic vitamin seems to promise definite hope of success as an agent for stimulating the growth of marasmic children. Hess has shown a similar effect of yeast vitamin, but our results do not permit, as yet, of conclusions as to the relative merits of the two sources of vitamins.

The dosage is not yet satisfactorily worked out and the conditions under which the effect is produced are not yet defined. These various features are under investigation and the results presented above are given as a stimulus to further work, rather than as conclusive evidence.

VARIATIONS IN INFANTS OF TOTAL BLOOD SOLIDS AND THE CONCENTRATION OF SODIUM CHLORID IN THE PLASMA *

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NEW YORK

In the course of some investigations at the Babies' Hospital on nutritional edema of infants, determinations of total solids of the blood and chlorid content of the plasma were made on a large number of children. Some interesting facts which were brought out in the course of this work are here presented. A discussion of the significance of the findings will not be attempted. Therefore, a review of the extensive literature on the osmotic pressure of the blood and the relation of blood water and salts to the fluids in the tissues, conditions which have been supposed to have some importance in the production of this form of edema, is hardly called for here.

The literature of the two subjects which are considered in this communication is very limited. We have been unable to find reported any results of chlorid determinations in the plasma of infants' blood. Also, very few figures are obtainable on total solids of the blood, although the subject has been discussed by many pediatrists. Lederer[1] determined the blood water of suckling dogs. Lust[2] has reported a number of observations on blood water of normal infants. His results will be referred to later. Gettler and Baker,[3] at Bellevue Hospital, have carried out a very complete investigation of the blood of normal adults. The results given for total solids and chlorid in the plasma of adults are of especial interest for comparison with the figures obtained by us for normal infants.

In all, seventy-nine determinations of blood solids and eighty-one of blood chlorid were made on sixty-seven different children. The ages ranged from 5 weeks to 6 years, but most of the subjects were under 2 years. Thirteen were well-nourished normal children from 2 months to 6 years of age; some of them were breast fed, some were fed with modifications of cow's milk and some were on a mixed diet. The remainder were suffering from quite a wide variety of diseases, the principal groups being lobar pneumonia, bronchopneumonia, tetany,

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* From the Laboratories of the Rockefeller Institute for Medical Research and the Babies' Hospital.

1. Lederer: Ztschr. f. Kinderh., 1914, **10**, 367.
2. Lust: Jahrb. f. Kinderh., 1911, **73**, 85 and 179.
3. Gettler and Baker: Jour. Biol. Chem., 1916, **25**, 211.

marasmus and intestinal disturbance, nutritional edema, sclerema, and one case of poliomyelitis. Three of the children had highly concentrated blood. The ages of the abnormal children corresponded closely with those of the normal children. The diet was various with these also.

Technic Employed.—About 5 c.c. of blood were drawn into a syringe. One portion was transferred to a platinum dish and the remainder to a tube containing about a gram of powdered potassium citrate. The portion in the platinum dish was used to determine the total solids. This was immediately weighed, evaporated on the waterbath, and dried to constant weight in an oven at about 100 C. Total solids are reported as per cent. by weight. The citrated blood was centrifugalized to separate the plasma from the cells. The protein was then removed from the plasma according to the method of McLean and Van Slyke for the determination of blood chlorid.[4] In the beginning their method was used for the determination of the chlorid in the filtrate. As identical results were obtained by the simpler Volhard method, however, most of the determinations of chlorid, after the preliminary removal of the protein, were made by the Volhard method. The figures are reported as grams of sodium chlorid in 1 c.c. plasma.

Normal Infants.—The results obtained with normal infants are shown in Table 1. Comparing the averages here with those of Gettler

TABLE 1.—Normal Children

Name	Date	Age, Months	Water in Blood, Per Cent. by Weight	Total Solids, Per Cent. by Weight	Chlorid in 1 C.c. Plasma Computed as Gm. of NaCl
Tessie R.	Oct. 6	54	82.39	17.61	0.00577
Julius H.	Oct. 10	48	82.43	17.57	0.00592
Helen H.	Oct. 10	72	81.83	18.17	0.00563
Lawrence S.	Oct. 23	20	82.23	17.77	....
Emmanuel D.	Oct. 23	14	82.35	17.65	....
John D.	Oct. 23	2	.....	.....	0.00626
Ralph S.	Oct. 23	5	83.69	16.31	0.00574
Ernest A.	Oct. 24	6	82.95	17.05	0.00641
Paul S.	Oct. 24	17	83.77	16.23	0.00577
Dorothy C.	Oct. 26	7	82.19	17.81	0.00595
Frank M.	Oct. 31	8	81.73	18.27	0.00600
Henry R.	Nov. 4	14	82.41	17.59	0.00536
John M.	Nov. 8	17	83.30	16.70	0.00577
Average			82.61	17.39	0.00587

and Baker for adults (Table 9), it is seen that the values for chlorid are almost identical, while those for blood solids show quite a marked difference, the range in infants being from 16 to 18, in adults from 20 to 25 per cent. of the total blood. Lust reports an average of 18 per cent. blood solids for normal infants, which agrees fairly well with our own findings. The range of values found for normal infants is narrower than that reported for adults, in respect both to blood solids and chlorid. A study of these findings does not reveal any correspondence between the variations in blood solid content and those in sodium chlorid in the plasma. The extreme values in each correspond to average values in the other.

4. McLean and Van Slyke: Jour. Biol. Chem., 1915, **21,** 361.

Determinations were made on the blood of a girl of 4 years 8 months, convalescent from infantile paralysis. These values are not included in any of the averages (Table 9). The sodium chlorid value is normal, that for blood solids much higher than the average for children.

Pneumonia. — Table 2 gives the results in four children with bronchopneumonia and in five children with lobar pneumonia, the ages

TABLE 2.—PNEUMONIA

Name	Date	Age, Months	Water in Blood, Per Cent. by Weight	Total Solids, Per Cent. by Weight	Chlorid in 1 C.c. Plasma Computed as Gm. of NaCl
BRONCHOPNEUMONIA					
Andrew N.	Oct. 10	15	82.05	17.95	0.00500
Joseph W.	Oct. 10	20	85.81	14.19	0.00534
Josephine C.	Oct. 13	10	82.90	17.10	0.00545
Carl H.	Dec. 21	12	82.43	17.57	0.00456
Average			83.30	16.70	0.00509
LOBAR PNEUMONIA					
Thomas W.	Oct. 10	30	83.71	16.29	0.00538
Gertrude G.	Oct. 10	33	83.66	16.34	0.00432
Rosemary D.	Oct. 10	10	82.62	17.38	0.00485
Isabella S.	Oct. 10	12	85.02	14.98	0.00473
Thomas L.	Dec. 20	15	81.99	18.01	0.00583
Average			83.40	16.60	0.00502

ranging from 10 to 30 months. The averages in the two groups are almost identical, both for solids and blood chlorid. But little importance is to be attached to the average for blood solids in either group, because of the wide variation met with. The average for blood chlorid is distinctly below normal; but there are two values in each group which are nearly normal. In the pneumonia cases as well as in the group of normal children there seems to be no correspondence between the variations in the blood solids and those in the sodium chlorid of the plasma.

Tetany.—The blood of ten children suffering from tetany of mild or severe type was examined. The ages ranged from 7 to 17 months. The results are shown in Table 3. The first four cases reported were

TABLE 3.—TETANY

Name	Date	Age, Months	Water in Blood, Per Cent. by Weight	Total Solids, Per Cent. by Weight	Chlorid in 1 C.c. Plasma Computed as Gm. of NaCl
Ferdinand E.	Dec. 21	17	82.39	17.61	0.00468
Edwin C.	Jan. 20	12	82.61	17.39	0.00549
Peter G.	Jan. 23	12	81.35	18.65	0.00482
Marcus C.	Mar. 28	14	.....	.....	0.00533
Edith McM.	Mar. 19	15	81.51	18.49	0.00458
Edith McM.	Mar. 22	15	79.34	20.66	0.00503
Rose G.	Dec. 1	17	83.18	16.82	0.00510
George I.	Dec. 1	9	84.67	15.33	0.00582
Billie C.	Dec. 19	13	81.28	18.72	0.00494
Mary S.	Jan. 12	7	82.52	17.48	0.00501
Gladstone F.	Mar. 28	14	.....	.....	0.00545
Average			82.09	17.91	0.00512

children with mild or moderate types of tetany; the remaining six all showed well-marked symptoms. The values for blood solids generally are higher than in normal children. The chlorid average is much lower than the normal, with only four values which even approximate it. No regularity can be seen in the relation of blood solids to the chlorid in the plasma in children with tetany.

Marasmus.—Table 4 shows the results of examination of the blood of twenty-three children suffering either from marasmus or from prolonged intestinal disturbance. The ages ranged from 5 weeks to 4 years, but most of the children were under 1 year. The average for blood solids is slightly below the normal average; that for blood chlorid very much below the normal. The range of values for blood solids, however, is very similar to that found in normal children. In this group, also, no regularity can be seen in the correspondence of blood solids and blood chlorid.

TABLE 4.—Marasmus and Intestinal Disturbance

Name	Date	Age, Months	Water in Blood, Per Cent. by Weight	Total Solids, Per Cent. by Weight	Chlorid in 1 C.c. Plasma Computed as Gm. of NaCl
Mary McG.	Sept. 30	6	83.26	16.74	0.00370
Mary McG.	Oct. 13	6	83.44	16.56	0.00540
Florence H.	Oct. 4	9	82.56	17.44	0.00519
Solomon B.	Oct. 4	12	83.02	16.98	......
Agnes L.	Oct. 4	6	82.96	17.04	0.00500
Salvatore L.	Oct. 4	5*	83.77	16.23	0.00523
Martin C.	Oct. 4	8	81.88	18.12	0.00454
John L.	Oct. 4	9	82.73	17.27	0.00442
Walter K.	Oct. 4	6	83.50	16.50	0.00468
Thaddeus E.	Oct. 4	6	83.63	16.37	0.00503
Edith F.	Oct. 6	6	83.07	16.93	0.00447
George N.	Oct. 6	3	83.90	16.10	0.00508
Leonie W.	Oct. 10	8	83.10	16.90	0.00412
Henrietta F.	Oct. 10	8	82.12	17.88	0.00500
Alfred D.	Oct. 10	7	81.37	18.63	0.00476
Alfred D.	Oct. 26	8	82.11	17.89	0.00576
August S.	Oct. 13	6	82.50	17.50	0.00478
James T.	Oct. 13	48	83.62	16.38	0.00396
Grace D.	Oct. 13	8	83.90	16.10	0.00515
Anna E.	Oct. 13	8	83.45	16.55	0.00500
Mary T.	Sept. 30	9	82.25	17.75	0.00412
Mary T.	Oct. 6	9	83.15	16.85	0.00353
John A.	Oct. 6	6	81.40	18.60	0.00461
John A.	Oct. 13	6	83.86	16.14	0.00412
Albert H.	Oct. 24	12	81.21	18.79	0.00483
Minnie C.	Jan. 13	16	83.63	16.37	0.00545
Thomas S.	Jan. 25	3	83.90	16.10	0.00560
Average			83.94	17.06	0.00475

*Weeks.

Concentrated Blood.—Three children among those examined showed abnormally concentrated blood. All of them had previously suffered from gastro-enteritis. In one, the blood concentration appeared to be the result of a transfusion; another had suffered from a severe burn; a third was deeply cyanosed at the time the blood was taken. The first and second cases had very high hemoglobin, in both instances reaching 140 per cent. The findings in these children are reported as a separate group in Table 5. Two examinations were made

TABLE 5.—CONCENTRATED BLOOD

Name	Date	Age, Month	Water in Blood, Per Cent. by Weight	Total Solids, Per Cent. by Weight	Chlorid in 1 C.c. Plasma Computed as Gm. of NaCl	Hemoglobin, Per Cent.
Bernard K. ...	Oct. 6	8	80.34	19.66	0.00318	...
William C.....	Oct. 4	1	77.12	22.88	0.00541	140
William C.	Oct. 13	1½	76.25	23.75	0.00412	140
Richard D. ...	Oct. 4	5½	80.37	19.63	....	140
Richard D.	Oct. 13	6	79.20	20.80	0.00536	
Average			78.66	21.34		

of the blood of each of the children with high hemoglobin. The five values given for blood solids show a wide range, but are all in a totally different class from those of all the other children studied. These values approximate the values for normal adults. The chlorid values vary so greatly that an average of the four would have little significance. It is worth noting that one extremely low value is found in a child who had received, on the preceding day, a large subcutaneous injection of bicarbonate of soda and more of the same drug by mouth.

Nutritional Edema.—In Table 6 are given the results of eleven determinations of blood solids and blood chlorid in five children suffering from nutritional edema. The ages ranged from 2 months to 2 years. The findings in this group show a strikingly low average for blood solids. In not a single instance is the value as high as the average given for normal children, and in only one is the value as high as the lowest in the normal group. The values for blood chlorid do not differ greatly from the values found in the other pathologic groups, the average being much below normal. The range, however, is wide, including several approximately normal figures.

TABLE 6.—NUTRITIONAL EDEMA

Name	Date	Age, Months	Water in Blood, Per Cent. by Weight	Total Solids, Per Cent. by Weight	Chlorid in 1 C.c. Plasma Computed as Gm. of NaCl
Seraphine C.	Sept. 30	24	86.28	13.72	0.00437
Seraphine C.	Oct. 13	..	84.93	15.07	0.00511
Seraphine C.	Nov. 14	..	85.51	14.49	0.00590
Mathilda F.	Sept. 26	15	85.21	14.79	0.00417
Mathilda F.	Oct. 4	..	83.53	16.47	0.00511
Mathilda F.	Oct. 13	..	84.70	15.30	0.00511
Mary F.	Oct. 10	3	87.30	12.70	0.00468
Mary F.	Oct. 14	..	87.09	12.91	0.00550
Louise S.	Oct. 30	4	84.92	15.08	0.00536
Louise S.	Nov. 6	..	.....	.....	0.00445
Marie K.	Jan. 20	31	87.29	12.71	0.00510
Average			85.68	14.32	0.00499

Sclerema.—Three children, aged 2 months, 4 months and 2 months, respectively, having sclerema, were examined. The results are given in Table 7. The average for blood solids in this group is somewhat below normal, but does not at all resemble that obtained in the group of nutritional edema. Blood chlorid in two of the cases is normal, in the third it is extremely low. An injection of bicarbonate of soda had been given to this child on the previous day.

TABLE 7.—SCLEREMA

Name	Date	Age, Months	Water in Blood, Per Cent. by Weight	Total Solids, Per Cent. by Weight	Chlorid in 1 C.c. Plasma Computed as Gm. of NaCl
James V.	Oct. 14	2	83.73	16.27	0.00274
George K.	Oct. 28	2	83.48	16.52	0.00575
Nathaniel D.	Oct. 31	4	83.23	16.77	0.00644
Average			83.48	16.52	0.00498

After Bicarbonate Injection.—During the investigation three children in all had received subcutaneously a bicarbonate of soda injection within the twenty-four hours preceding the blood examination. The findings are grouped together in Table 8. The sodium bicarbonate

TABLE 8.—AFTER INJECTION OF SODIUM BICARBONATE

Name	Date	Age, Months	Injection	Water in Blood, Per Cent. by Weight	Total Solids, Per Cent. by Weight	Chlorid in 1 c.c. Plasma Computed as Gm. of NaCl
John A.	Oct. 13	6	Oct. 11—120 c.c.	83.86	16.14	0.00412
Bernard K.	Oct. 6	8	Oct. 5—240 c.c.	80.34	19.66	0.00318
James V.	Oct. 14	2	Oct. 13—120 c.c.	83.73	16.27	0.00274

injection may possibly have been the cause of the extremely low values here seen for chlorid in the plasma, but, on the other hand, several other children, in the marasmus and intestinal disturbance group, who had not received such an injection show similarly low values. In this connection a recent communication by K. Goto,[5] on blood studies in uranium nephritis in the dog and the protective action of sodium bicarbonate, is of interest. He finds that the increase of chlorid in the plasma observed in uranium nephritis is not so great when sodium bicarbonate is administered at the time.

After Saline Injection.—In ten children a physiologic salt solution had been injected subcutaneously shortly before the blood was studied. Although most of these findings have been included in the preceding tables, particularly that of the marasmus cases, they are presented together in Table 9. In two children the blood was examined shortly

TABLE 9.—AFTER INJECTION OF PHYSIOLOGIC SALT SOLUTION

Name	Date	Age, Months	Injection	Water in Blood, Per Cent. by Weight	Total Solids, Per Cent. by Weight	Chlorid in 1 c.c. Plasma Computed as Gm. of NaCl
Salvatore L.	Oct. 4	1	Oct. 3— 90 c.c.	83.77	16.23	0.00523
John L.	Oct. 4	9	Oct. 3—120 c..c	82.73	17.27	0.00442
Thaddeus E.	Oct. 4	7	Oct. 3—120 c.c.	83.63	16.37	0.00503
Grace D.	Oct. 13	8	Oct. 12—240 c.c.	83.90	16.10	0.00515
John A.	Oct. 6	6	Oct. 5—120 c.c.	81.40	18.60	0.00461
Seraphine C.	Nov. 6	25	Nov. 5—240 c.c.	84.42	15.58	0.00618
Mary McG.	Oct. 4	6	Oct. 2—240 c.c.	82.69	17.31	0.00626
Nathaniel D.	Oct. 31	4	Oct. 30—120 c.c.	83.23	16.77	0.00644
Alfred D.	Oct. 26	8	Before injection	(82.11)	(17.89)	(0.00576)
Alfred D.	Oct. 26	8	Oct. 26—240 c.c.	.....	.....	0.00583
Albert H.	Oct. 24	12	Before injection	(81.21)	(18.79)	(0.00483)
Albert H.	Oct. 24	12	Oct. 24—240 c.c.	83.16	16.84	0.00539
Average				83.21	16.79	0.00545

5. Goto, K.: Jour. Exper. Med., 1917, **25**, 693.

before and again a few hours after the hypodermoclysis. All these children show a somewhat lowered average for blood solids, but it is not lower than the values found for several children in the normal group, and it is very near the average found in the pneumonia and the sclerema groups. The average for chlorid in the plasma after saline hypodermoclysis is approximately normal. Since all the children who received hypodermoclysis belonged to the abnormal groups, in which blood chlorid is invariably lower, it seems evident that the injection of the saline raises the chlorid content of the plasma. Of the two children whose blood chlorid values before the hypodermoclysis were obtained, the one who showed a normal value before, showed practically no change after the injection; while the one who was below normal before the injection was brought almost to normal by it.

It is difficult to draw any definite conclusions as to the effect of diarrhea on the blood solids and chlorid. Nearly all the children with marasmus or intestinal disturbance had had more or less diarrhea. It might be expected that the blood water would be reduced, but this does not seem to be regularly the case. This group shows the lowest average found for blood chlorid. Except two cases in which soda bicarbonate had been injected, this group also includes all the very low values found.

An examination of Table 10 shows how great the tendency is for blood solids to remain constant. Only two groups show any significant

TABLE 10.—Summary of Tables

	Water in Blood, Per Cent. by Weight, Average	Total Solids, Per Cent. by Weight		Chlorid in 1 c.c. Plasma Computed as Gm. of NaCl	
		Range	Average	Range	Average
Gettler and Baker, adults.....	77.6	20.0 –24.9	22.4	0.00500–0.00637	0.00592
Normal infants	82.61	16.23–18.27	17.39	0.00536–0.00641	0.00587
Infants with pneumonia	83.35	14.19–18.01	16.65	0.00432–0.00583	0.00505
Infants with tetany	82.09	15.33–18.72	17.91	0.00458–0.00582	0.00512
Infants with marasmus, etc...	82.94	16.10–18.63	17.06	0.00353–0.00576	0.00475
Infants with concentrated blood	78.66	19.63–23.75	21.34	0.00318–0.00541	0.00452
Infants with nutritional edema.	85.68	12.70–16.47	14.32	0.00437–0.00590	0.00499
Infants with sclerema	83.48	16.27–16.77	16.52	0.00274–0.00644	0.00498
Child, 4 yrs. 8 mos., convalescent from infantile paralysis........................	80.85	....	19.15	....	0.00594

variations from the normal. The children with nutritional edema seem to have a greatly diluted blood, while those with abnormally high hemoglobin have a greatly concentrated blood. All the other pathologic groups show blood solids not greatly different from the normal values for infants.

The most striking point brought out by this investigation is the fact that almost all children not in a normal condition have a remarkably low value for chlorid in the plasma. Only one of the normal children shows a value as low as most of the high values of the other groups. This child, H. R., though perfectly normal at the time of

examination, had suffered a year before from severe marasmus. Of the children in the pathologic groups that show values as high as normal, most had received a saline injection during the twenty-four hours preceding. A few other exceptions to the rule are found in some particularly well-nourished children in the pneumonia and tetany groups. It must be emphasized, however, that on the whole chlorid in the plasma is extremely low in children not in normal condition, especially if they are poorly nourished and suffering from digestive disturbances.

CONCLUSIONS

1. The normal infants studied had about the same concentration of chlorid in the plasma as normal adults; the average for total solids in the blood was about 5 per cent. lower in infants than in adults.

2. In pneumonia there was irregularity in the values found, both for total solids and chlorid in the plasma, which is difficult to account for.

3. Children suffering from tetany showed a tendency to slightly higher total solids and higher chlorid in the plasma than was found in any of the other pathologic conditions studied.

4. Children suffering from malnutrition and digestive disorders showed the lowest chlorid in the plasma of all those investigated.

5. Children with nutritional edema all showed abnormally dilute blood, with chlorid in the plasma much below normal, though not lower than that of other sick infants.

6. Infants with sclerema had nearly normal total solids in the blood, with chlorid in the plasma like that of the other pathologic cases, excepting the marasmus group.

7. There was no constant relation between the variations in total solids of the blood and those in chlorid of the plasma.

8. Saline hypodermoclysis seemed to affect the percentage of total solids very little, but to raise the chlorid in the plasma nearly to normal.

9. In general, all infants not in normal condition had low blood chlorid, frequently very much lower than normal, but, except in edema, or under some unusual condition of blood concentration, the percentage of the total solids in the blood of infants tended to remain constant.

RUMINATION IN THE FIRST YEAR OF LIFE *

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If one looks up the literature on rumination in infancy, he receives the impression that the condition is an extremely rare one, not only because of the paucity of reports, but also because of the extensive way in which single cases are treated, and the discussion of them.

So far as I have been able to find, the first mention of rumination in infancy, aside from the very cursory remarks in textbooks, is the report of Freund[1] in 1903. He speaks of a small number of cases of rumination, which he regards as closely related to pylorospasm. There is no definite report of single cases in his article. Since then there have appeared in the literature reports of cases by Maas,[2] Finkelstein,[3] Pouliot and Moricheau-Beauchant,[4] Wirtz,[5] Mayerhofer,[6] Sluka,[7] Lust,[8] Brüning,[9] Huldschinsky,[10] Aschenheim,[11] Lehnerdt,[12] Schippers,[13] Wanietschek,[14] and Strauch.[15] With the exception of Freund, we see that none of these has reported more than two cases. The number of cases observed by Freund is, of course, not definitely known. This represents a total of known cases of sixteen. The condition could hardly be overlooked after one's attention is called to it. It is so definitely characteristic, and so easily diagnosed, that errors in diagnosis should be extremely few. This, therefore, is not the reason why so few cases have been reported. The answer must be either that the cases are extremely rare, or else that they have not been recognized,

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1. Freund: Mitt. a. d. Grenzgeb. d. Med. u. Chir., 1903, **11**, 325.
2. Maas: Med. Klin., 1907, **3**, 926.
3. Finkelstein: Lehrbuch der Saüglingskrankheiten, Berlin, 1908, II, Abt. I, p. 133.
4. Pouliot and Moricheau-Beauchant: Bull. Soc. de pédiat. de Paris, 1909, **11**, 88.
5. Wirtz: München. med. Wchnschr., 1910, **57**, 960.
6. Mayerhofer: Therap. Monatsh., 1912, **26**, 262.
7. Sluka: Wien. klin. Wchnschr., 1912, **25**, 288.
8. Lust: Monatschr. f. Kinderh., 1912, **10**, 317.
9. Brüning: Arch. f. Kinderh., 1913, **60**, 116.
10. Huldschinsky: Ztschr. f. Kinderh., 1913, **8**, 363.
11. Aschenheim: Ztschr. f. Kinderh., 1913, **8**, 161.
12. Lehnerdt: München. med. Wchnschr., 1914, **61**, 1977.
13. Schippers: Ztschr. f. Kinderh., 1914, **10**, 92.
14. Wanietschek: Jahrb. f. Kinderh., 1915, **82**, 66.
15. Strauch: Jour. Am. Med. Assn., 1915, **65**, 678.

because it would hardly seem from the literature that the cases were of such a nature as not to be worthy of special attention.

From the experience of the writer it would seem that the condition is much more frequent than is ordinarily supposed, and that the reason for not recognizing it is that the attention of the pediatric world in general has not been called to the condition in such a way as to bring it definitely before them. The following six cases, which were observed during a period of three years, one of which was previously reported by Strauch, constitute my reasons for believing that the condition is overlooked. It is desirable that this should not be the case, since rumination in infancy is an exceedingly fatal condition, and one about which we know extremely little. It is, therefore, desirable to be better informed on this subject, and to recognize all cases when they appear, in order to be in a position to study the condition more intensely and endeavor to arrive at some definite conclusions as to causation and treatment.

REPORT OF CASES

Case 1 (78293).—Christine B., aged 8 months, entered Presbyterian Hospital April 30, 1914. The present complaint was that the baby was unable to retain its food; took it readily, but soon began to vomit; had been slightly constipated. The child gained very little in weight. It was fed on breast milk up to three and one-half months, and was then weaned because the physician thought the milk probably did not agree with the child. Feeding, on entrance, consisted, in the twenty-four hours, of 10 ounces of whole milk, 6 ounces of gruel, 1¾ teaspoonfuls of magnesium citrate. It had never been sick before, except for a slight cold, and the family history was negative.

Aside from extreme emaciation, the examination showed nothing. On entrance the child weighed 8 pounds 3½ ounces. She was put on an albumin milk mixture, which was gradually increased up to May 24. During that time her temperature tended to be definitely subnormal, at times going as low as 97 F. During her entire stay at the hospital she regurgitated in a peculiar way. The milk was brought up into the mouth, often following sucking of the fingers. It was held there and gargled, usually a considerable amount of food being spilled out. This was done after every feeding, sometimes a few minutes, sometimes longer. The treatment consisted, first, of strychnin, $\frac{1}{500}$ grain hypodermatically, four times a day, until May 4. Gastric lavage was given from May 2 to May 11, with apparently no benefit. From May 4 until May 24, bromids were given without effect. During this period on albumin milk feeding, the child showed a weight which was practically stationary, May 24 having a weight of 7 pounds 15½ ounces, a loss of 4 ounces in twenty-five days. The food was then changed to a modified albumin milk, which was thickened with flourball. This was continued until June 4 without any apparent effect on the child's health. Water, during this time, was supplied by means of continuous normal salt enemas, up to May 31. From May 28 strychnin was given, and June 3 bromids were again given. June 4 the child's weight was 7 pounds 14½ ounces. The change of food had apparently had no effect on the rumination. In fact, from June 4 there was a rapid decline in weight, so that on June 9 the infant weighed only 7 pounds 1 ounce, at which time the child left the hospital. Nothing further was heard of the patient. At no time was increased peristalsis noted.

Case 2 (79139).—Caroline D., aged 4 months, was brought to the hospital by her mother June 8, 1914, because she failed to gain in weight. The child

weighed practically the same as when she was born. From a few days after birth she had been fed every two hours with diluted milk, proportions unknown. Appetite good. She had vomited but little. Vomiting had not been a marked feature of the trouble. She always showed a tendency to constipation, so that it was necessary to give laxatives, and usually magnesium citrate was added to the food. The child was very restless and slept poorly. She was a full term child and the birth was normal. Examination showed a child considerably underweight, very fretful, but apparently not very sick. No palpable glands; throat was negative; heart and lungs negative; abdomen negative, as were the extremities. July 21 she was first noticed to ruminate, which occurred several times in succession. This was only noted on one or two occasions, and immediately cleared up. Later, the child developed a pyelocystitis of moderate degree, and on August 5 a slight prolapse of the rectum. She left the hospital September 15, without showing any other signs of rumination. No increased gastric peristalsis was noted.

In this case the first rumination was noticed July 21. Thereafter this occurred not more frequently than once a day, and rarely that often. No rumination was noted after August 4.

Case 3 (83073).—Liebe S., aged 13 weeks, previously reported by Dr. Strauch.[15]

Case 4 (98449).—Kasmera S., aged 7 months, entered the Presbyterian Hospital Oct. 2, 1916, because of vomiting and loss of weight. The birth was normal, the birth weight was unknown. The child nursed at the breast for four and one-half months, every two hours or oftener, and was taken off the breast because the physician said the food did not agree with the child. The child was then put on Horlick's malted milk, 3 teaspoonfuls to 4 ounces of water every three hours, with which it was fed for one month. It was then put on condensed milk, half milk and half water, 4 ounces every three hours. To this 4 ounces was added ½ teaspoonful of sugar. The child vomited a little at every feeding while on the breast, but during the month previous to entrance, the mother thought that the child had vomited almost the entire feeding. During the summer, which was exceedingly hot, the child had had an attack of diarrhea, with fifteen green mucous stools a day. The father and mother are living and well. One other child is well. No miscarriages. On examination there was noted a greatly emaciated child, with the skin hanging loose. On first examination, definite signs of rumination were noted. In the neck there was a slight adenopathy. The chest and lungs were all right; there were a few palpable axillary glands; abdomen distended, especially in the epigastrium; intestines slightly distended. The liver was at the border of the ribs; the spleen was not palpable. Aside from emaciation, the extremities were negative. The child was put on albumin milk during its stay in the hospital, which was until October 14. During this time the temperature showed a marked tendency to be subnormal, averaging between 97 and 98 F. On entrance the weight was 7 pounds 2 ounces, which on October 13 had dropped to 6 pounds 14 ounces, and on the 14th, or day of death, the child's weight had risen to 7 pounds 5½ ounces.

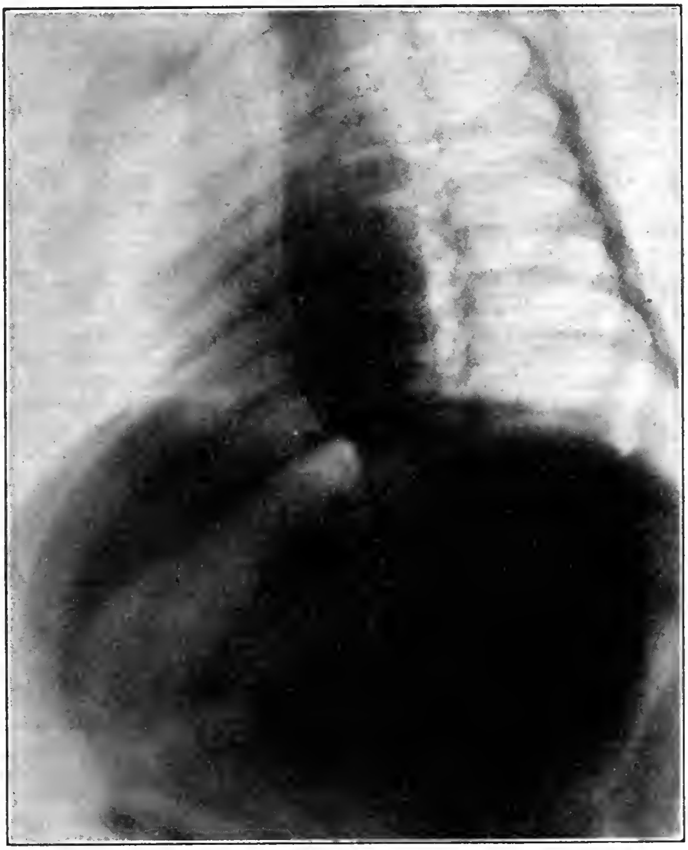
In this child, with the change of food, the treatment of Strauch of plugging the nostrils was tried faithfully, but seemed to have no effect whatever on the rumination, which was very severe, occurred after every feeding, and resulted in the expulsion of a large amount of the food taken in. Gastric lavage seemed to have no effect. The blood and urine showed nothing special. Roentgen-ray examination showed dilatation of the lower end of the esophagus (see illustration).

It was possible in this case to get only a partial necropsy. Such as it was, the report is as follows:

The stomach was found to have an exceptionally large fundus. The pyloric half was very small and narrow. The cardia was 2.5 cm. wide; 3 cm. above the cardia, 2.3 cm. wide. It was 8 cm. from the cardia to the pylorus. The

tip of the fundus was 5 cm. from the cardia, and it was 11 cm. from the tip of the fundus to the pylorus. Absolutely no cardiac sphincter muscle could be made out on gross examination. The pyloric sphincter was normal.

Microscopic examination of the stomach showed that the mucosa was intact throughout all the sections and presented no changes other than early post-mortem digestion. In sections taken from the cardia, the fundus and the pyloric portion, the arrangement and thickness of the musculature appeared normal (Raulston).



Roentgenogram of patient, Case 4, showing dilatation of the lower end of the esophagus.

Case 5.—Baby C., aged 5 months, was seen by me March 9, 1915, in consultation with Dr. Renaud. The history was as follows: The child was born at full term; normal delivery; weight at birth, 10 pounds. It was nursed at the breast for three months. For the previous two months it had been given malted milk and cow's milk, with sugar and water. The child was first noticed to vomit on March 1. The vomited matter had been the food which the child had taken. There had been a definite tendency toward bringing the food up into the throat, holding it there a while, spilling over, and then swallowing again; in other words, a definite history of rumination. In the beginning of the vomiting, the child had lost rather rapidly, but had not been weighed at

the time of consultation, so it is not known how much the loss in weight had been. There had been no previous diseases, except a slight cold. There were no brothers or sisters. There was a slight neurotic tendency on the father's side. The mother was rather nervous.

On examination, an emaciated child was seen, very cross and quite easily disturbed. After taking food it was noticed that the food was brought up into the mouth, gargled for a short time, some of it spilling over, and then swallowed. This was repeated rather frequently. No gastric peristalsis was noted at this time, nor later, as reported by Dr. Renaud.

The diagnosis of rumination was made, and I suggested the treatment of Strauch by means of plugging the nostrils. This was not carried out, but after determining the nature of the disease, two other measures were followed: Immediately after the taking of food, when the child would start to regurgitate, its attention was attracted for some fifteen to twenty minutes, after which it was left alone; to do this, a little bell was rung, or some such procedure was resorted to. The child was given ⅛ grain chlorbutanol (chloretone) and 5 grains stronthium bromid every two to three hours.

According to the report, the child gained in weight quite rapidly, and on March 25 weighed 12½ pounds and rumination had ceased. The child after a year had shown no tendency to return to its former condition, and was a perfectly well, normal child, walking around and doing such things as any other child of its age should do.

Case 6 (10223).—Mary K., aged 7 months, entered the Presbyterian Hospital in the care of Dr. Winnolt Feb. 9, 1917. The history was that she had shown an inability to gain weight; some vomiting; frequent green curdy stools. She was a full term baby, vertex presentation, normal labor; birth weight, 8¼ pounds. For the first three months the infant gained weight steadily and then remained stationary. She had always vomited. She vomited not only immediately after nursing, but also at intervals up to the time of the next feeding. Occasionally this vomiting was projectile, but this was only once in awhile. For the first five months she was fed on breast milk entirely. Up to three months the breast had been given every three hours, then the interval had been lengthened to four hours, with the idea of decreasing the vomiting. During the fifth month the milk supply began to grow low, and her weight remained stationary and the vomiting became, if anything, worse. At five months the bottle feeding was begun. At first skim milk and water, equal parts, 7 to 8 ounces every three hours, were given. At this time the breast milk suddenly gave out. For two weeks skim milk was given, then cream was added, but on the cream mixture the vomiting was worse, so that the cream was stopped. After this, dextrimaltose was added to the skim milk. At five months the weight was 12 pounds, the same as that at three months. Dextrimaltose was used for two weeks. After that, Mellin's food for two weeks. For awhile she did not seem to vomit on this, but very soon the vomiting commenced the same as previously. She was then given condensed milk, 3 teaspoonfuls to 7 ounces of water every three hours at first, and then every four hours, with the addition of albumin water twice a day, which was begun a week before entrance. She gained half a pound on this, but soon lost it again.

There was no history of severe colds, fevers, or coughs. As to the stools, usually when a new food was first given the stools were normal. Later they seemed to become curdy and often green. There had been no mucus in the stools just previous to entrance, but when the child was on the breast there had been a great deal. Stools had recently been about five a day. They had never been hard. The child slept well, and, as a rule, did not waken at night. There was one older child. There was no tuberculosis in the family, and there had been no miscarriages.

Physical Condition: The patient was seen to be a fairly well nourished female infant, but somewhat undersized and under weight. The eyes, ears, scalp, nose and mouth were normal; no generalized lymph adenopathy; epi-

trochlear glands not palpable. The lungs and heart showed nothing abnormal; liver and spleen not palpable, nor was there any palpable mass in the abdomen; no visible gastric peristalsis. The weight on entrance was 11 pounds 12 ounces.

The child was put on a feeding of albumin milk, 35 ounces; cane sugar, ¾ ounces; malt extract, ¼ ounce; water, 7 ounces—six feedings of 7 ounces each. There was slight variation of this diet, the change being mostly in the shift from cane sugar to dextrimaltose, and an increase of the malt extract. Final feeding, albumin milk, 36 ounces; dextrimaltose, ¼ ounce; malt extract, ¾ ounce; barley water, 6 ounces—six feedings of 7 ounces each.

The temperature during the infant's stay in the hospital was within normal limits, except for a short period from February 22 to 26, when the child had an acute coryza. On entrance the blood showed: red blood cells, 4,530,000; whites, 7,900; hemoglobin, 75 per cent. There was a slight leukocytosis of 12,500 during the acute coryza. The urine throughout was negative. On February 12 it was first noticed that the child regurgitated some material into the mouth, which process was preceded by a sucking movement. After a few moments the child would swallow and the material would be regurgitated. On the 13th the child showed a very definite rumination at 8:30 in the evening. This lasted for about five minutes. On the 14th rumination was again seen, and this time the stomach was seen to assume a definite shape, and there were a few slight peristaltic movements. This rumination was noticed not oftener than twice a day, and continued, gradually decreasing in frequency, the last being noted February 19. On March 16 the weight was 12 pounds 14½ ounces, a gain since February 9 of 1 pound 2½ ounces.

We have, then, a case of a slight degree of malnutrition, accompanied by a rumination of not very great severity. This rumination, without any further treatment than a proper regulation of diet, gradually disappeared and had not returned over a period of practically a month. During a stay of five weeks in the hospital the child gained over a pound in weight, and in every way was in satisfactory condition.

DISCUSSION

In the cases found and reported by me, certain phenomena have seemed to be suspiciously common. The first of these is ulcer of the duodenum. This can probably be explained on the basis of an ulcer, due, as Helmholz[16] has already mentioned, to a streptococcus infection in a very depleted individual. It is altogether likely that the frequent presence of duodenal ulcer in these cases is not in itself of any etiologic importance, but rather is a complication or sequel of the condition. Of quite a different nature is the picture of pylorospasm. This has been described in too large a proportion of cases to be overlooked. It occurred in the cases of Lust, Case 2 of Aschenheim, and in that of Strauch. When we consider that the condition is perhaps not noted in a fair proportion of cases, we can regard this as a rather large percentage. Whether there is any connection between the definite tendency to increased muscular action of the stomach and the relatively decreased resistance of the cardia, is yet to be determined. The Roentgenogram accompanying Case 4 of this series shows a very definite dilatation of the esophagus of a spindle-shaped character, just above the cardiac orifice of the stomach. So far as I have been able to find,

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16. Gerdine and Helmholz: Am. Jour. Dis. Child., 1915, **10,** 397.

this has not been reported before in infants. This is almost exactly similar to the condition which we find in cardiospasm, which Sippy has already pointed out. In cardiospasm in adults, the constriction does not occur at the cardiac orifice of the stomach, but just above it. This would seem to be the case in this instance. Most authors have been satisfied with the statement that the condition is a motor neurosis of the stomach. This hardly classifies rumination, nor distinguishes it from pylorospasm. We would expect, if it were only a motor neurosis of the stomach, that the reactions would remain in the stomach itself, but as we see, from the one case reported here, there is definite relaxation of the wall of the esophagus, with resultant dilatation. It seems to me that the whole condition would be best explained on the hypothesis of Hess[17] that the circular involuntary muscles all have a tendency to spasm in certain individuals, and that pylorospasm is only one isolated condition with which many others may be and often are associated. If the primary condition were a pylorospasm, the food after being forced back through the cardiac orifice might, through its irritation of the esophageal mucous membrane, produce a constriction in the lower end of the esophagus, with the result that the food is held in the esophagus, and that the gargling movements of the child result. As all of us know, overaction of the stomach musculature is not necessarily accompanied by visible gastric peristalsis. In fact, gastric peristalsis is only of significance when it is definitely visible, and is accompanied by vomiting, projectile in type. It would, therefore, seem to me that an hypothesis which would cover the needs in this instance would rest on a general tendency toward overaction of the involuntary circular muscles, with the primary action in the stomach from a pylorospasm (the term being used in the wide sense), the food then being forced back into the esophagus, the cardiac orifice of the stomach being closed by the overaction of the muscles of the lower end of the esophagus, with rumination resulting, rumination ceasing when these muscles have relaxed.

SYMPTOMATOLOGY

In general, we may divide these cases into two types, the mild and the severe. We will probably find cases which vary in severity, so that any hard and fast line may not be drawn between these two. In the mild type the rumination occurs only at long intervals, perhaps once or twice a day, and then is not so marked as to be accompanied by any definite loss of food. This condition usually responds readily to proper hygiene and feeding, and causes very little anxiety. Far different, however, is the severe case. Here we find a nervous, emaciated, pale

17. Hess: Am. Jour. Dis. Child., 1914, **7**, 184.

child, which cries rather easily and does not sleep well. The food which is given the child is well taken; in fact, greedily taken, and as a rule the stools show no special variation from the normal. Soon after the bottle is taken, the child begins to bring the food up. The food when brought into the mouth is gargled for a short time and then swallowed. This may happen again and again, the interval between the attacks being exceedingly short. The probable danger in this process is not in the process itself, but in the resultant loss of food through spilling over. In this condition an exceedingly large proportion of the food may be lost, so large a proportion, in fact, that the remainder may be, and frequently is, insufficient to support life. These attacks may occur at any time between feedings, and have been recorded by Schippers as occurring even during sleep. A very large proportion of these children die. Of those reported, the patients of Finkelstein, Lust, Lehnerdt and Strauch died. This, together with my Case 4, makes a mortality of almost 25 per cent.

As to the fate of many of the cases, we are doubtful, because they were not followed long enough; as, for instance, Case 1, reported in this series. Of the severer cases, certainly more than 25 per cent. of the infants die; probably as many as 50 per cent. die.

Aside from the symptoms of rumination, the children bear very great resemblance to severe cases of pylorospasm or of marasmus.

TREATMENT

The treatment as projected has been principally along three lines:

1. Drug treatment. This has consisted in giving bromids and other sedatives for this condition, and in using cocain and local anesthetics on the stomach. It may be said that there is no reason to think that such drug treatment will be successful in any great number of cases.

2. Dietetic. This has consisted largely in giving the child a thick vegetable puree or cereal gruel. In a few cases this has seemed to be of value, but in many it has utterly failed.

Strauch has suggested that the nostrils be plugged with wax in order to stop breathing, and thus reduce the tendency to rumination. This does not seem a logical procedure to us, and after having tried it in two cases we have abandoned it. In neither case did the plugging of the nostrils bring any result. In many cases washing of the stomach and introducing the food by means of a tube has been tried. This has been abandoned as not bringing definite results. It was tried in most of our cases with, apparently, no success.

3. I am inclined to feel that the idea of Schipper's is probably the best in regard to these cases, and that is the treatment of the psychic condition of the child. All unnecessary excitement should be avoided,

the child should be screened from its immediate surroundings, but immediately after taking food it would be well to draw its attention to some object, such, for instance, as a small bell or some plaything, to keep it absolutely distracted from any thought concerning the rumination. It seemed to me that this, more than anything else, was the cause of the ready response to treatment in Case 5.

CONCLUSIONS

1. Rumination is probably a much more frequent condition than is ordinarily supposed.

2. The condition can be explained on the basis of a hyperexcitability of the involuntary muscles, as suggested by Hess.

3. Treatment to be successful should probably be based on attention to the psychic condition of the child.

GLIOSARCOMA IN AN INFANT OF SEVEN WEEKS, RESEMBLING HYDROCEPHALUS *

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History.—Simon K., 7 weeks old, was admitted to the Babies' Hospital Jan. 16, 1917; only child, of Russian parentage; family history negative; full term; normal labor; birth weight reported, 6 pounds, 5 ounces. Breast fed to date of admission.

When about 2 weeks old the parents first noticed that the head was enlarging more rapidly than normal. A little later the veins of the scalp began to be very prominent. Both of these symptoms had increased steadily up to date of admission. There had been frequent vomiting and rather loose stools. The child had not thrived, but had apparently been failing in nutrition.

Physical Examination.—On admission, the child was fairly well developed but wasted. Compared with the small body, the head was enormous. The general appearance of the patient was that of a child with a hydrocephalus. Measurements were:

Circumference of head	51 cm.
Circumference of chest	39 cm.
Circumference of abdomen	34 cm.
Length of body	52 cm.

The head was somewhat asymmetrical, there being a very great prominence in the left frontal region. The scalp was covered with a network of enormously dilated veins. The skin of the scalp was tense and shining, especially over the most prominent portion. The sutures were widely separated. There was slight internal strabismus and occasional nystagmus; conjunctivae were normal; the knee jerks were present and active; no evidence of paralysis. The cry was feeble; the color good. There were no other deformities, and the examination of the abdomen and thorax was negative.

Course.—During the next few days the head increased greatly in size. The rapidity of the growth can best be indicated by the child's weight; in spite of the steady wasting of the body, the weight increased 650 gm. during the nine days of observation. The urine was negative. A spinal puncture showed a fluid under increased pressure containing 120 cells per c.mm., 63 per cent. of these being polymorphonuclears and 37 per cent. lymphocytes; the globulin test was positive. The temperature was most of the time subnormal. Food was taken badly and the bowels were loose.

Over the frontal eminence the scalp became very tense and thinner, till on the eighth day a spontaneous rupture took place over this prominence, followed by a discharge of a considerable quantity of cerebrospinal fluid, the amount of which it was difficult to estimate, but it probably did not exceed 150 c.c. The opening in the scalp appeared about 9 cm. long. The rupture was followed by a protrusion of brain substance—a true hernia cerebri. The child grew steadily

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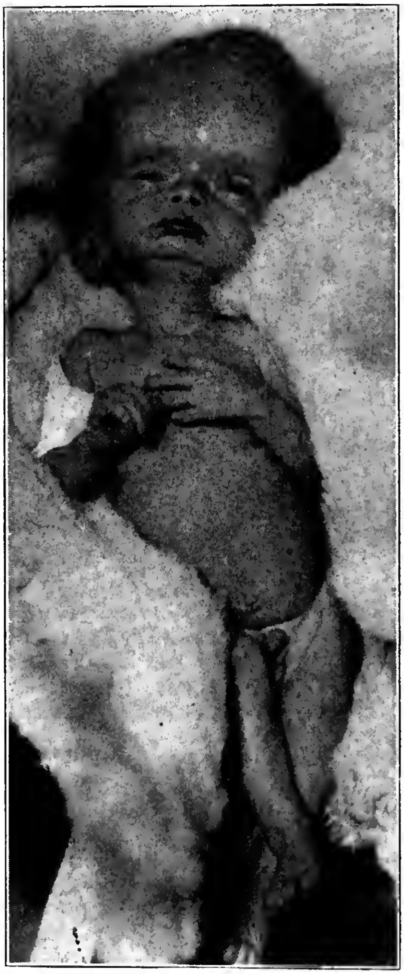
weaker and death occurred two days later from exhaustion. There were no convulsions.

Necropsy.—The head measured 48.5 cm. in circumference. There was a rupture in the scalp and dura through which protruded cranial contents forming a mass 8 by 5 cm. in size and weighing 145 gm. The cerebrospinal fluid was but slightly in excess—not over 90 c.c. being present. The dura showed many punctate hemorrhages. The brain showed marked asymmetry, the left hemi-



Gliosarcoma of the brain.

sphere being fully three times the size of the right. The tumor mass involved practically the entire left hemisphere; it was a soft, lobulated new growth containing in its substance many softened areas, many recent hemorrhages and yellow pigmented remains of old hemorrhages.

While removing the brain the protruding mass forming the hernia cerebri broke off. This made up only a small part of the tumor. The

tumor apparently grew from the floor of the lateral ventricle and increased in size until it was enveloped only by a thin shell of the compressed cortex which varied in thickness from 1 to 5 mm. It involved the left hemisphere only. In the right hemisphere the convolutions were markedly flattened from pressure and there was moderate distention of the lateral ventricle, but no new growth was present. The cerebellum was compressed to about one-half normal size. After removal the left hemisphere measured 19.5 by 14 by 3 cm.; the right, 10.5 by 8.5 by 7.5 cm.

A microscopic examination of the tumor by Dr. Martha Wollstein, pathologist to the hospital, showed it to be a gliosarcoma. A complete autopsy was made but the examination of the other organs showed no new growths or any other lesions having any relation to the cerebral condition.

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THE EFFECT OF COD LIVER OIL ON GROWTH IN A CASE OF "INTESTINAL INFANTILISM" *

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Greatly retarded growth, amounting to a condition of infantilism, is occasionally seen as a result of certain prolonged derangements of the functions of digestion, as well as a consequence of organic changes in these organs. The exact nature of the changes which bring about arrested growth in the first mentioned group of cases is as yet little understood, but it has generally been connected with disturbances in the metabolism of calcium, magnesium and phosphorus. Negative balances in these substances have repeatedly been found in children belonging to this class.

Because of the demonstrated effect of cod liver oil in increasing the retention of these inorganic salts in other conditions, particularly in rickets, it was determined to try its effect on the patient whose history is here reported, in whom the diagnosis of infantilism of intestinal origin was tentatively made.

REPORT OF CASE

History.—Elizabeth R., aged 8½ years, came first under observation Feb. 9, 1916; her condition may be described in a word as "infantile," her weight being but 29 pounds net and height 39⅛ inches, or that of an average child of about 3 years. She was the eldest of three children, the other two being normal and well developed, a sister of 6 years being 4 inches taller and 12 pounds heavier than the patient. The parents were healthy and lived in a suburban town in excellent surroundings. The child had always had the best of home care.

Early progress was quite normal. She was born at term, weighing 8 pounds; was nursed for twelve months and did very well; muscular development was average. Weaning was easy and feeding for the second year not at all difficult. In fact, up to nearly 2 years of age, except that her stools were much of the time very pale, her progress was considered satisfactory. The food given at that time was chiefly milk, about 50 ounces being taken daily in five meals; she was also given beef juice, eggs and orange juice.

Ever since she was 2 years old the child had suffered from digestive symptoms, though she had never had acute attacks either of diarrhea or dysentery. Occasional vomiting was present during the first two years, but after that time vomiting attacks became more frequent, recurring every few days, and very

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often she would vomit during the night. The stools were always pale and were reported large in proportion to the food taken; at times she was constipated, but much of the time the stools were reported "frothy" in character, but no blood and rarely much mucus was present. There was always much gas in the bowels. Abdominal distention had been an almost constant symptom and most of the time it was extreme.

The diet had been much restricted. From the end of the second year milk had been excluded, also green vegetables, soups, cereals and fruits. Until a few months before her visit she had been fed chiefly on rare meat, eggs, toast and butter and a large amount of potato. For the last few months small quantities of milk had been added to the diet. The appetite was usually fair, but she constantly craved highly seasoned food and such articles as onions, strawberries, ice cream, lemons, green corn, etc.

The child had never had any acute illness except an attack of grip a few weeks before. Her progress mentally had been nearly that of the average child. On the whole, the mother considered her condition as rather better for the preceding six or eight months than previously, the abdominal distention had been much less and the stools of better character, but vomiting still occurred about twice every week.

No records of the weights had been kept; the following were given by the mother from memory:

At 12 months, 19 pounds; 3 years, 24½ pounds; 4 years, 30 pounds; 8 years, 30½ pounds (her best weight).

There were also no records of her height, but the mother thought that for the preceding two or three years there had been little or no growth.

Physical Examination.—On examination she appeared physically like an average child of 3 or 3½ years. The body was thin, but was in no sense wasted. The child was symmetrically small—trunk, face and extremities. The head was well formed and showed no irregularities or abnormalities; fontanel closed. Hands and feet, legs and arms were quite normal; facial expression, intelligent; speech and mental development were like that of an average child of 6 or 7 years. Physical examination of heart and lungs was negative. The circulation was rather poor; extremities much of the time cold. In the abdomen were found no abnormal masses; there was no distention. The liver and spleen were not palpable. Superficial glands were slightly enlarged. The tongue was coated; the breath now, and usually, sweet; the temperature was normal. There was moderate beading of the ribs, and very slight epiphyseal enlargement, but no signs of active rickets were present. The teeth, twenty in number, were in poor condition; several were carious.

Measurements: Weight, 29 pounds net; height, 39⅛ inches; head, circumference, 19¼ inches; chest, circumference, 20 inches.

Though she had suffered almost constantly from digestive symptoms since 2 years old, there did not seem to be in the diet a sufficient explanation for the arrested growth.

Metabolism Observations.—February 27 the child entered the Babies' Hospital for metabolism observations. She was given the same diet in variety and amount which she had been taking for several weeks previously. Though the quantity of food was small, it was all she would take at the time. The diet was as follows:

Breakfast: One egg; 2 slices toast; 2 gm. butter; 2 gm. sugar; one-half gm. salt.

Dinner: Scraped beef, 60 gm.; 15 c.c. beef juice; one-half small baked potato; 120 c.c. milk; 2 gm. sugar; 1 gm. salt.

Supper: Toast, one-half slice; 120 c.c. milk; 2 Huntley & Palmer breakfast biscuits; 2 gm. butter; 2 gm. sugar.

Was given 60 c.c. water at each meal and all she would take between meals. Total calories in her food, 650.

Weight on beginning metabolism observations was 12.5 kilos (27½ pounds); she was thus receiving at this time but 52 calories per kilo.

In Table 1 are given the average daily intake and excretion for the three days of metabolism observations.

TABLE 1.—Metabolism Observations, First Period—Feb. 23-26, 1916

	Grams, Daily Average								
	Nitrogen	Fat	CaO	MgO	P_2O_5	Cl	K_2O	Na_2O	Total Ash
Intake..............	5.8398	24.176	0.5049	0.1802	1.3052	1.4279	1.4438	0.8593	5.4532
Excreted in feces...	0.7551	11.218	0.7043	0.1525	0.7219	0.0655	0.5075	0.0534	2.2425
Absorbed..........	5.0847	12.958	—0.1994	0.0277	0.5833	1.3624	0.9363	0.8059	3.2107
Excreted in urine...	4.2200	......	0.0181	0.0582	0.7149	1.2212	0.6523	1.0638	3.5802
Retained...........	+0.8647	12.958	—0.2175	—0.0305	—0.1316	+0.1412	+0.2840	—0.2579	—0.3695
Per cent. of intake retained..........	14.77	53.65	...... —43.1	...... —16.9	...... —10.1	9.88	19.7	...... —30.0	...... —6.77

Dried weight of feces, average daily, 18.53 gm.

On this restricted diet the child had relatively large, constipated, but well-digested, stools. The metabolism balances showed a fair nitrogen and fat retention, but a very striking loss in mineral salts, only potassium and chlorin showing a positive balance. The abnormal loss took place chiefly through the feces.

For how long a period such a disturbance of salt metabolism had existed it was of course impossible to say, but the negative balances found coincided with the clinical history of the case. Something which would aid in the absorption of salts, particularly calcium and phosphorus, or lessen their excretion through the intestine was evidently what was needed. Even though there were no evidences of active rickets, it was decided to try the effect of cod liver oil as soon as the condition of the digestive organs warranted it, and at the same time to increase the salt intake by giving more food, particularly more milk.

At the end of a month the mother reported that the child had vomited but twice, that she was eating much better and was now able to take besides her other food, 360 c.c. of milk daily. The bowels were now quite regular. Cod liver oil with maltine (a preparation containing 30 per cent. oil) was begun about April 1, 1 teaspoonful twice daily, the dose being gradually increased until at the end of a few weeks she was taking 2 teaspoonfuls three times daily, this being equivalent to about 8 c.c. of the pure oil daily. This amount was continued up to the end of August, a period of about five months. It was then omitted for two months.

In June, July and August she suffered from a moderate attack of whooping cough. During this period the appetite was poor, but she "took her food as a duty," the mother reported. In spite of these adverse conditions the gain in weight was steady, so that by the end of August she was 5 pounds above her low weight early in March. With the subsidence of the whooping cough the appetite returned and her gain in weight was now rapid. The net weights during the summer were as follows:

June 9, 31½ pounds; August 25, 32½ pounds; September 28, 36½ pounds; November 1, 40 pounds.

The diet was practically the same as that mentioned above, except that the milk had been increased to 500 c.c. daily. Much difficulty was experienced in making her take vegetables; the only one she would take was carrots.

The next opportunity for an examination of the child was on November 10. Her measurements were as follows:

Weight, 41¼ pounds; height, 41½ inches; head, circumference, 19¾ inches; chest, circumference, 22½ inches.

This represented a gain in nine months of 2⅜ inches in height and of 2½ inches in circumference of chest, and in weight of 13¾ pounds in eight and a half months. The improvement in the general condition was striking; though still very small, she was plump and well nourished; the tongue clean; the abdomen slightly distended; the circulation excellent. She was able to walk a mile a day.

For three weeks during the latter part of November, with an attack of bronchitis, the appetite was lost and her digestion was considerably upset; she vomited occasionally; the bowels became loose and the same light colored "foamy" stools previously mentioned returned. In this attack she lost nearly 4 pounds in weight.

December 12 she entered the hospital a second time for metabolism study; observations were continued for a three-day period, beginning December 15. Her weight on admission was 37 pounds 6 ounces. The body was well nourished; color good; child good natured and happy; very much more active than during her previous admission. Her stools were formed, in fact, rather constipated, a daily enema being required; they were of a grayish-yellow color, but well digested.

She continued on the same diet which she had been taking at home, which was as follows:

Breakfast: One egg on 1 piece of toast, thinly buttered; 200 c.c. milk; 1½ slices graham bread and butter.

Dinner: Graham bread, 1½ slices, with butter; 2 tablespoonfuls scraped beef; 1 small baked potato with 1 ounce beef juice; 200 c.c. milk.

Supper: One slice white and 1 slice graham bread with butter; 200 c.c. milk.

Two teaspoonfuls of cod liver oil with maltine were, as before, given after each meal. Total calories given estimated at 1,030, making 61 per kilo or 28 per pound.

The intake, excretion and balances for this metabolism period are given in Table 2.

TABLE 2.—Metabolism Observations, Second Period—Dec. 15-18, 1916

	Grams, Daily Average								
	Nitrogen	Fat	CaO	MgO	P_2O_5	Cl	K_2O	Na_2O	Total Ash
Intake	8.5701	43.382	1.3283	0.3821	2.6311	3.4650	2.3624	2.6159	11.9358
Excreted in feces	1.4090	14.642	1.0994	0.3163	0.7450	0.1586	0.5841	0.2560	3.5217
Absorbed	7.1611	28.740	0.2289	0.0661	1.8861	3.3264	1.7783	2.3599	8.4141
Excreted in urine	5.3390	......	0.0174	0.0513	1.3950	2.7840	1.0312	2.1192	6.7092
Retained	1.8221	28.740	0.2115	0.0148	0.4911	0.5424	0.7471	0.2407	1.7049
Per cent. of intake retained	21.3	66.3	15.9	3.87	18.6	15.65	31.6	9.2	14.3

Dried weight of feces, average daily, 31.5 gm.

This showed, as compared with Table 1, a somewhat increased retention of nitrogen and fat; but the most striking changes were in the salt balances. Instead of a negative balance in total ash of 6.77 per cent., there was a positive balance of 14.3 per cent. All the salts showed positive balances. The most marked changes were in the calcium where a negative balance of 43.1 per cent. was changed to a positive balance of 15.9 per cent.

Six weeks after leaving the hospital, in spite of intercurrent varicella and a mild otitis, the mother reported that she had never known her in better health; she had regained her weight lost during the bronchitis. A report late in March stated that she was in excellent condition except slight stiffness of the legs (rheumatism?) which she had suffered from in previous cold seasons.

The effect of cod liver oil and phosphorus in increasing the calcium and phosphorus retention in rickets has been known for a number of years. The careful observations of E. Schloss,[1] Schabad,[2] Birk[3] and many others[4] have established this fact beyond question. It has been repeatedly noted in our own observations at the Babies' Hospital. In a recent case the figures for the per cent. of the intake of the different salts absorbed and retained were as follows:

	CaO		P_2O_5		K_2O	
	Absorbed	Retained	Absorbed	Retained	Absorbed	Retained
Before cod liver oil and phosphorus...	16.6	14.0	51.5	18.0	74.2	12.9
After cod liver oil and phosphorus...	45.1	43.8	88.3	33.0	87.3	23.8

The value of the phosphorus in the combination is questioned by Schloss, though Schabad considers it important. Exactly how it is that the cod liver oil acts, has not yet been clearly shown. It certainly creates conditions which allow the calcium intake to become incorporated into the organism.

From Schloss' observations it would seem to be essential that there should be ample intake of calcium in order to obtain benefit from the cod liver oil. He found, for instance, that with a rachitic breast-fed infant the administration of cod liver oil and phosphorus did not improve the condition; but that when calcium acetate was added great improvement followed. It is undoubtedly true that the intake may be low in some breast-fed infants; but it is almost always adequate in those who are artificially fed.

In a later communication, Schloss states that calcium-phosphorus preparations alone with breast feeding are almost as effective in improving the calcium and phosphorus balances as when they are used with cod liver oil. The simple inorganic salts, he believes, added to breast milk as a food, work better than the natural salts of cow's milk, even when cod liver oil is added. His conclusion is that the nature of the food and the condition of absorption in the body are of even more importance than the form of salt addition.

In the patient under consideration there were but slight evidences of old rickets and none whatever of any active rickets. The cod liver

1. Schloss, Ernst: Jahrb. f. Kinderh., 1913, **28,** 694.
2. Schabad, J. A.: Monatschr. f. Kinderh., 1911, **9,** 659; **10,** 12; 1912, **11,** 4.
3. Birk, W.: Monatschr. f. Kinderh., 1909, **7,** 450.
4. Review of Rickets. Berl. klin. Wchnschr., 1916, **50,** 1340; **51,** 1366.

oil was administered with the hope, but without very much expectation, that it might influence salt retention. At the same time, by increasing the diet, especially the amount of milk, an attempt was made to increase the salt intake. The results in this case far exceeded our expectations and they showed conclusively how essential to proper growth is the assimilation of the salts ingested.

There are certainly several factors that must be considered in explaining the improvement in this patient. An improved digestion from the omission of certain disturbing articles of food, an enlarged diet, particularly the addition of the milk, the cod liver oil, and possibly the preparation of malt with which it was administered — any one or possibly all of these were factors in the result. It is our own belief that the cod liver oil was by far the most important one, the next being the milk.

Whether children like the one whose history is here given are likely to reach a normal physical development, is a question of great interest. We know from the studies of Osborne and Mendel on rats that growth may be arrested by deficient feeding for very long periods, and then by proper feeding, growth and development may be resumed until the normal is reached. They found, however, that there was a period beyond which, if the deficient feeding was continued, growth was not resumed. There are, then, certain limitations to growth which cannot be exceeded. All children like this one need to be closely watched, and, if possible, metabolism observations made from time to time to determine the result of the feeding.

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HUNGER IN THE INFANT *

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Cannon and Washburn,[1] and Carlson and his colaborers have given us a proved method for studying hunger objectively; its time of occurrence, its intensity, its effects, and the means by which it may be produced or inhibited. They have shown that contractions of the so-called empty stomach cause the hunger sensation. These contractions depend in part on vagus tonus. They can be increased by chemical changes in the blood, but are primarily due to a gastric mechanism as purely automatic as is that of the heart.

Impulses set up by these contractions and carried to the higher centers are, in the normal consciousness, recognized as hunger. These impulses produce secondary effects such as restlessness and irritability. They increase the reflex excitability of the central nervous system, the heart beats faster, and there are changes in the vasomotor mechanism. Well fed, sedentary adults seldom experience hunger. The prime factor in their desire for food depends not on the basis of distress due to the contractions of a hollow viscus, but on "the memory processes of past experience with palatable foods." This psychic factor is appetite, and its absolute distinction from the physical factor, hunger, must be kept in mind.

Working on dogs, Patterson, in 1914, showed the gastric hunger contractions to be much more frequent and vigorous in young than in older animals. In 1915, Carlson and Ginsburg described the great intensity of hunger contractions in the human new-born. Previous to that year no productive analytic studies of the hunger sense in the human infant had been made. Appetite and hunger were not distinguished, and the sucking mechanism alone had been analyzed.

In 1888, Auerbach distinguished the infantile type of sucking from the voluntary inspiratory type employed by the adult, and in 1894 Basch, disproving the older theory of Preyer that sucking is instinctive, showed it to be entirely reflex.

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1. All references to the literature will be found at the end of the article.

Czerny, in 1893, observed that an infant awakened a short time after taking his fill from the maternal breast, would again suck vigorously if placed on it, and concluded that sucking per se could not be considered as a sign of hunger. A few years later (1900) Keller wrote that, since the normal infant sleeps three hours after nursing, although its stomach is empty in two hours, the emptying of the stomach cannot be considered a positive criterion of need for food. Pies, in 1910, considered the reddening and eczema of the lower lip which occurs in undernourished infants as a sign of hunger, and referred it directly to the infant's fruitless sucking. In 1913 Schlossmann concluded from extensive observations on semistarved infants that the sensation of hunger exists only in the imagination.

Meyer and Rosenstern studied the results of starvation in the different types of alimentary disorder, recording particularly the pulse, temperature, respiration and weight changes. Rosenstern later (1911-1912) wrote extensively on the general subjects of hunger and inanition in infancy. These studies are all defective in that they do not distinguish the various factors concerned. Neumann, Pfaundler, Cramer, Süszwein, Barth, and Kasahara have discussed the subject of disturbances in the food urge largely from the point of view of imperfections in the sucking mechanism.

The present studies are concerned particularly with the gastric factors in the urge for food. The major of these, the hunger contractions, was studied by means of apparatus similar to that used by Carlson. A rubber balloon of about 20 c.c. capacity attached to one end of a small soft rubber catheter is inserted into the stomach and inflated, the catheter is attached to a bromoform manometer with a cork float and a writing pennant which records the gastric movements on smoked paper.

The material investigated included 5 premature infants weighing from 1,200 to 2,500 gm., 40 full term new-borns under 3 weeks of age, and 11 older babies, 5 between 1 and 2 months, 2 between 3 and 4 months, 3 between 4 and 6 months, and 1 boy of 2 years with a surgically induced gastric fistula made necessary by the effects of corrosive in the esophagus. The gastric movements of some of the infants were recorded only once; on others as many as twenty observations were made.

Carlson and Ginsburg refer to the readiness with which most infants accept and retain the tube and balloon. It is naturally impossible to secure a graphic record of the stomach movements of a raging infant. Carlson and Ginsburg did their work on full term new-borns. These infants, as a rule, sleep quietly when not disturbed. The present work was carried on in a dimly lighted, quiet room. I had less difficulty when the infant was left undisturbed in his crib than when I

attempted innovations, such as threading a pacifier on the tube or having the infant held in the nurse's arms.

The older babies resent the presence of the tube, and with them it was often necessary to make repeated attempts to secure tracings. Some infants finally became accustomed to the presence of the tube and slept quietly, particularly if the experiments were conducted in the evening. Most of the tracings on the 2-year-old boy with the gastric fistula were made when he was awake. The greatest problem was to keep him sufficiently interested to prevent crying and restlessness and at the same time to prevent riotous hilarity. In his case the balloon was introduced directly through the fistula.

It is said that passage of the stomach tube in infants is apt to cause aspiration pneumonia. No ill results followed the procedure carried out in these studies.

Does the presence of the balloon in the stomach act mechanically to produce gastric contractions? Carlson states definitely that it does not, and gives the following reasons for his belief:

1. The presence of the distended balloon in the stomach between the contraction periods does not induce these contractions.

2. In Mr. V. [his gastric fistula case] the gastric contractions can be observed directly through the large fistula without any balloon in the stomach.

3. The contraction periods come on just as frequently without any balloon in the stomach and produce the same effect (hunger).

4. In pigeons the periodic strong contractions of the empty crop can be seen directly through the skin, and a balloon in the crop does not alter their frequency or intensity.

The results of this work fully confirm Carlson and Ginsburg's report that the stomach of the new-born infant exhibits greater hunger contraction than does that of the adult. The intervals between the contraction periods are often less than five minutes and usually not longer than from ten to twenty minutes. The first contraction period after a nursing is apt to consist of from five to twenty separate contractions and to last from two to eight minutes. The succeeding contraction periods frequently endure from thirty minutes to an hour or even longer. The duration of each contraction is about twenty seconds. In many of the infants the contraction time of the more powerful contractions, especially in those periods ending in partial tetanus, was about eighteen seconds. Except in the first contraction period after a nursing, endings in partial tetanus were frequently observed. Partial tetanus is sometimes present before the close of the period. With the apparatus used, the force of the single contractions usually sufficed to raise the column of bromoform 2 to 3 cm. During partial tetanus the bromoform may be raised 5 cm.

Patterson found practically continuous hunger contractions in premature pups. It is particularly easy to obtain graphic records of the

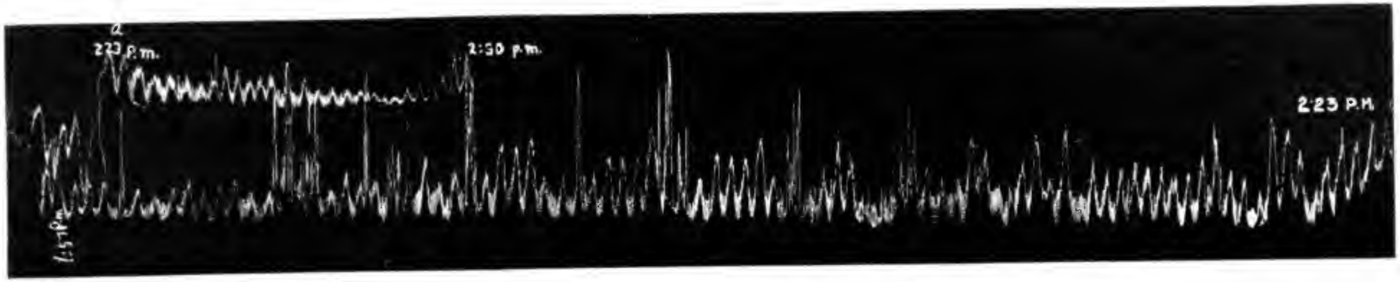

Fig. 1.—Hunger contractions in normal, new-born infant. Beginning of partial tetanus at extreme right in lower tracing.

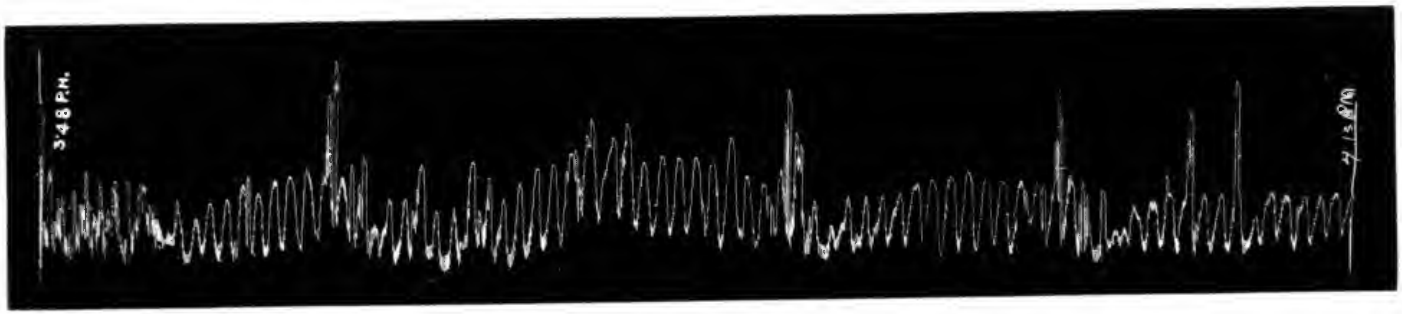

Fig. 2.—Prematurely born infant. Typical activity of the premature baby's stomach. Boy F., aged 15 days; weight, 1,536 gm.; getting 45 c.c. breast milk six times a day. Previous feeding at 2:30 p. m.

hunger contractions of the somnolent, prematurely born infant. The stomach of such an infant is in a state of nearly continuous contraction. The individual contractions require about the same length of time for their completion and are as powerful as those of the full term infant. In a tracing begun forty minutes after a feeding of 15 gm. of breast milk to a premature baby (Baby 5) weighing 1,510 gm., the record appears very like that obtained by Rogers from the crop of a pigeon in the second day of starvation. The periods of contraction last two or three minutes, with intervening periods of quiescence of about the same length. The individual contractions last twelve to fifteen seconds and raise the bromoform column 3 to 4 cm. Partial tetanus is frequent. Nine days later, when the infant was receiving more food, in spite of the fact that he had not gained in weight and that the tracing was begun five hours after his last feeding, the record obtained was similar to those from other infants.

Are the hunger contractions more frequent or more powerful in cyanosed infants? May they furnish a stimulus for crying with consequent better aeration of the lungs? In two such cases no significant increase or decrease in the hunger contractions could be observed. No records were taken from any cyanosed premature infants, although such infants are frequently slightly blue for the first few days.

Carlson, working on the adult, was unable to produce hunger contractions by any sort of stimulus acting directly in the mouth or in the stomach, except that he occasionally could, by suddenly distending the stomach, produce a few transitory contractions. He found, uniformly, that the only effect of such local stimulation was inhibitory. In general, the taste of salt, sour, bitter, or sweet; or the chewing of agreeable, disagreeable, or indifferent substances, all produce temporary inhibition of the gastric contractions. Chewing palatable foods by the adult when hungry causes an inhibition, made more lasting by the flow of appetite juice in the stomach.

Carlson found that acid and alkaline solutions, food and liquids in the stomach, all inhibit the hunger contractions. Inhibition from the stomach is less transitory than that from the mouth. Boldyreff showed that the periodic contractions of the empty stomach were inhibited by the presence of acid in the intestine. Brunemeier and Carlson completed and enlarged this work. They demonstrated inhibition from the presence of gastric juice or acid chyme in the small intestine. This inhibition from the stomach and intestine is reflex, partly through Auerbach's plexus, but mainly through the long reflex arc with the efferent path to the stomach muscles through the splanchnics.

Inhibition from the mouth is not present in the frog (Patterson). Carlson, who suspects that such inhibition involves conscious cerebral processes, has suggested experiments in infants to settle the point.

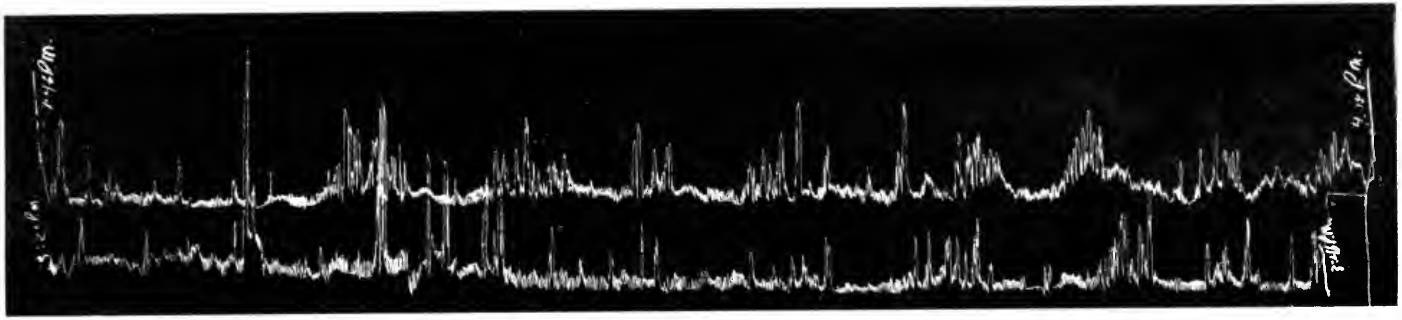

Fig. 3.—Prematurely born infant; shows numerous short, forceful contraction periods. Boy Von, 4 days old; weight, 1,510 gm.; birth weight, 1,715 gm.; at 2: 30 p. m. received 15 c.c. breast milk.

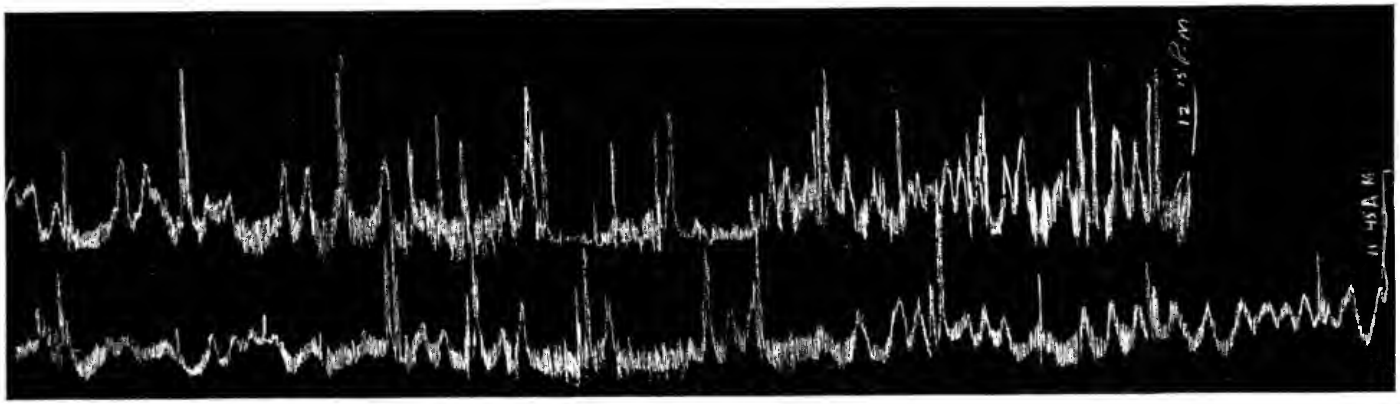

Fig. 4.—Baby Mi., 15 days old; tracing shows presence of hunger contractions in an infant who nursed poorly.

Repeated trials with breast milk, sugar water, common salt, quinin, and lemon juice in the mouths of premature and new-born infants in my study failed to produce inhibition of hunger contractions.

In general I obtained the same results in an infant of 8 weeks. A transitory inhibition occurred occasionally when sugar water was placed in his mouth. In none of the infants did chewing or sucking on the thumb or tube produce inhibition. Nor did such movements or the presence of sugar, breast milk or other substances in the mouth induce hunger contractions.

The boy of 2 years showed inhibition when sugar or protein milk (his diet at the time) was placed in his mouth. Quinin, dilute hydrochloric acid, small amounts of sugar water, table salt in crystals or solution, did not inhibit. Benzosulphinidum solution inhibited twice. It was not used subsequently. The sight of sugar did not inhibit. He began to cry when he saw his bottle if the latter were not given him immediately. Conseqeuntly the effect of his seeing the bottle on the hunger contractions could not be registered. During the periods of quiescence the sight of the nurse who fed him did not induce hunger contractions, although he began to whine and tease when she entered the room.

Apparently inhibition from the mouth was produced by those substances only which the child regarded as food. Quinin very evidently made a profound sensory impression, but did not inhibit the contractions. Dilute hydrochloric acid did not inhibit, while unsweetened protein milk (which is slightly sour) did.

Carlson's hypothesis as to the need of conscious cerebration for the production of inhibitory reflexes from the mouth would appear to offer the correct explanation. It seems to be agreed that the new-born infant leads a subcortical reflex existence (Soltmann-Cramer). Kussmaul and Thiemich note that the new-born infant accepts sugar and rejects salt, food that is sour and bitter — action which is almost certainly purely reflex on the part of the infant.

My work shows that when 20 c.c. of water or milk are introduced into the stomach during a contraction period inhibition follows invariably. This was found true in infants of all ages. With small amounts of water the inhibition often lasted only three or four minutes, when the contraction period would be resumed.

On the other hand, it was not unusual to recover from 15 to 40 cm. of clotted milk through the stomach tube even an hour after vigorous hunger contractions had begun. This is a considerable portion of the infant's meal, and in these cases would represent from one-sixth to one-fourth of his total intake at the previous feeding. Soltmann showed that the inhibiting nervous mechanism of the heart is much less effectual in the new-born infant than in later life. It seems possible

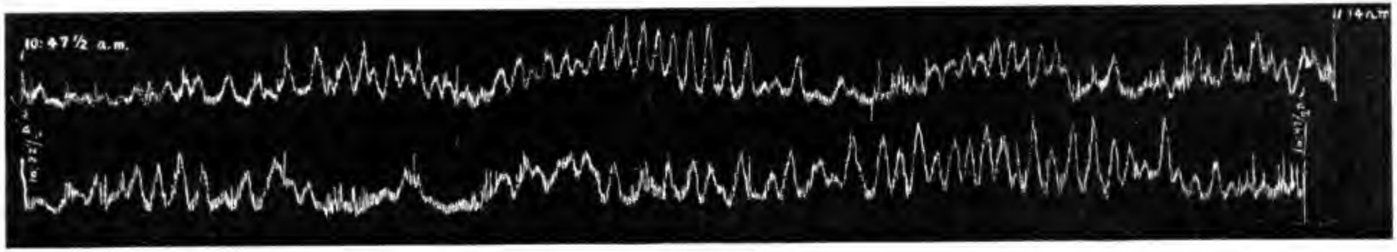

Fig. 5.—Baby Ri., 6 days old, with congenital myxedema; tracing shows presence of hunger contractions in a babe who nursed poorly.

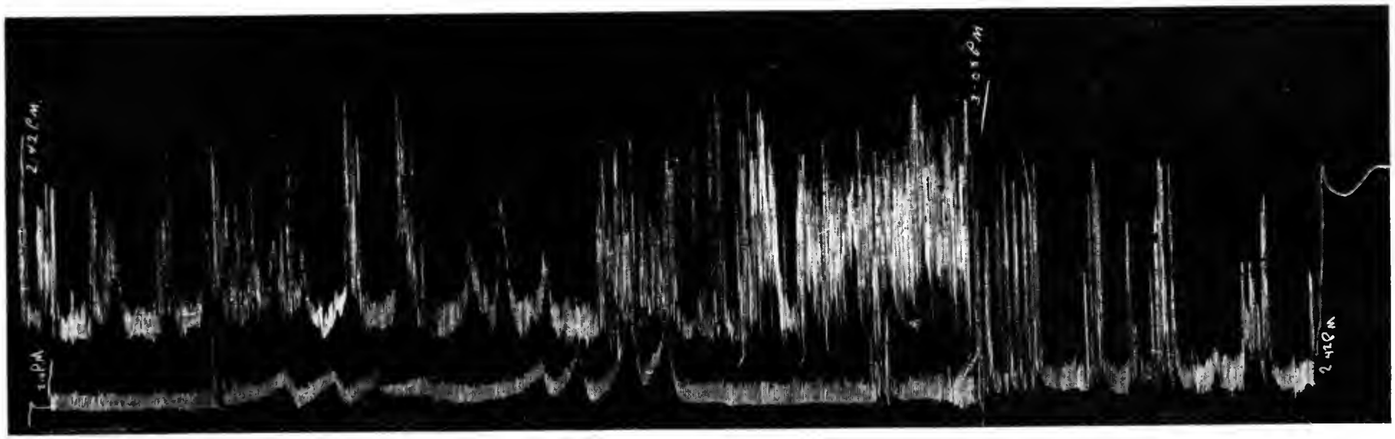

Fig. 6.—Baby J., 4 months old. Tracing shows development of hunger contractions during the interval following a feeding.

that the nervous apparatus for the inhibition of the gastric hunger movements may likewise be immature. Or the tissue hunger may be so great as to overcome any but the strong inhibition of a heavily laden stomach and duodenum.

The vagi form the sensory pathway from the stomach to the brain. The first reflex centers are the sensory nuclei of the vagi in the medulla. A second center, possibly that for conscious hunger, is located in the optic thalami. Rogers has shown that the picking reflex in the pigeon (analogous to the sucking reflex in the babe) is abolished on removal of the thalami.

The reflex irritability (as indicated by the knee jerk) is increased synchronously with each hunger contraction (Carlson). No observations have been made on the infant's knee jerks during the hunger state; but Zybell has shown that the electrical irritability increases during the first eighteen hours of starvation.

Let us summarize the events from the close of one meal till the end of the next. The infant sleeps. The upper stomach musculature maintains a tonic grasp on the contained food. The pyloric antrum is traversed by peristaltic waves (Cannon). The stomach gradually empties. The point of origin of the peristaltic waves rises higher and higher. The tonus rhythm of the fundus begins. The stomach empties itself more completely, the tonus rhythm becomes more intense, and the first hunger contractions appear (Rogers and Hardt).

The first contraction period is apt to be short. After a wait of perhaps twenty minutes a longer and more intense hunger period arrives; then another and another. The infant's sleep becomes lighter. He is more easily awakened by external stimuli or by gastric discomfort. He is put to the breast, nurses vigorously, becomes fatigued (Schmidt, Cramer, Pfaundler), or experiences satiety from distention (Neisser and Bräuning) and again goes to sleep.

What constitutes the hunger state? Does it result from the summation of impulses with an increasing psychic and reflex irritability? The evidence is to the contrary. The increase in the reflex excitability is synchronous with the contraction phase of the stomach, and is absent in the intervals between the contractions. In the infant who has been some hours without food the hunger contractions are nearly continuous, and it would be expected that the reflex excitability would be nearly continuously high.

In the absence of hunger contractions the infant often sucks vigorously on the tube attached to the balloon. The receptive mechanism for the institution of the sucking reflex is so delicate that it is impossible to provide, artificially, a minimal stimulus. During the hunger state, when presumably a rapid succession of hunger contractions maintains a low reflex threshold, there may often be observed a succession of

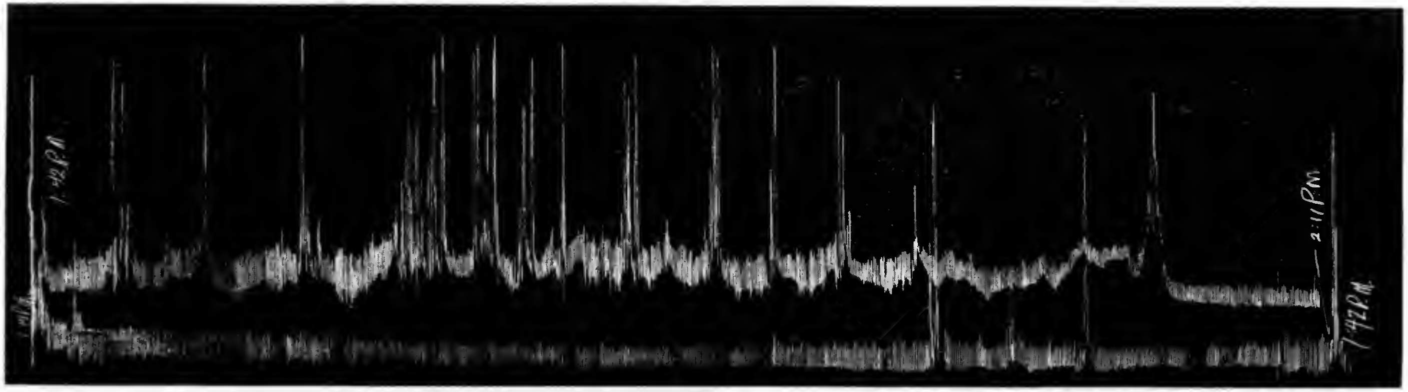

Fig. 7.—Same as Figure 6.

automatic sucking movements involving the lips, tongue and lower jaw, each movement providing the necessary stimulus for its successor.

The lay mind is prone to think that the crying infant is hungry. Comby and Czerny and Keller believe that hunger is a minor cause of crying. Rosenstern notes that in hunger young babies are usually quiet, but that the older infants cry more. Schlossmann remarks that the normal infant endures hunger well.

Observations on this point extending over sixteen months of study of the hunger sensation lead me to believe that in normally thriving breast fed infants, except when more than three or four hours have elapsed since the last feeding, neither the hunger contractions themselves nor the increased irritability due to them are ordinarily immediate factors in the production of crying. Young infants sleep throughout strong contraction periods. Older infants often do the same, and are frequently quiet even from twelve to sixteen hours after a feeding. Mental factors produce crying at a very early age. And the fact that crying ceases when food or water is administered may only mean that the infant's attention is diverted to the performance of a pleasurable act.

It may be noted in this connection that the 2-year-old boy was happier when allowed to take food into his mouth, and that his outlook on life was much more cheerful on days when he could take nourishment by mouth than on other days when the esophageal constriction increased, and it became necessary to introduce the food through the gastric fistula. This feeding through the fistula was without pain, and the child submitted to it with some pleasure.

What is the time interval between feeding and the first appearance of gastric hunger contractions? Ginsburg, Tumpowsky and Carlson studied this point in thirty normal breast fed infants under 4 weeks of age. They gave no data as to gain in weight and did not determine the amount of food taken, but stated that the babes nursed till satisfied. They found the average time between nursing and the appearance of hunger contractions to be two hours and forty minutes, with a minimum of two hours and twenty minutes and a maximum of three hours and thirty minutes. My observations on twelve new-born infants under like conditions yielded these results; a minimum of one hour and thirty minutes, a maximum of three hours and thirty minutes, and an average of about two and one-half hours.

Many infants in the first two weeks do not receive a sufficient supply of breast milk. This is particularly apt to be true of the time the babe and the mother remain in the hospital. Consequently, observations made under the conditions so far outlined may be misleading. Table 1 (A, B and C) gives the results of all satisfactory tracings obtained from normally thriving babies on whom sufficient data as to food intake and weight gain were obtained.

TABLE 1.—INTERVAL FOR DEVELOPMENT OF HUNGER

A. PREMATURE INFANTS

Name	Age, Days	Food	Feeding Interval	Quantity at Feeding	Interval Before Tracing	Time for Development of First Hunger Period	Remarks
Sw.	7	Breast milk	4 hours 5 times a day	35 c.c.	None	40 min.	Premature Wt. 2,140 gm.
Sw.	11	Breast milk	4 hours 5 times a day	50 c.c.	20 min.	1 hr., 20 min.	Wt. 2,240 gm.
Sw.	20	Breast milk	4 hours 5 times a day	90 c.c.	52 min.	2 hours	Wt. 2,470 gm.
Sw.	25	Breast milk	4 hours 5 times a day	75 gm.	38 min.	1 hr., 50 min.	Wt. 2,565 gm.
St.	13	Breast milk	4 hours 5 times a day	30 c.c.	None	1 hour	Premature Wt. 2,270 gm.
St.	14	Breast milk	4 hours 5 times a day	50 c.c.	None	40 min.	Wt. 2,280 gm.
St.	25	Breast milk	4 hours 5 times a day	90 c.c.	1 hr., 13 min.	1 hr., 15 min.	Wt. 2,450 gm.
St.	28	Breast milk	4 hours 5 times a day	90 c.c.	38 min.	1 hour	Wt.
St.	36	Breast milk	4 hours 5 times a day	100 c.c.	32 min.	1 hr., 50 min.	Wt. 2,720 gm.
Fre.	9	Breast milk	4 hours 6 times a day	45 c.c.	1 hr., 38 min.	1 hr., 38 min.	Premature Wt. 1,380 gm.
Fre.	15	Breast milk	4 hours 6 times a day	45 c.c.	1 hr., 18 min.	1 hr., 18 min.	Wt. 1,530 gm.
Fre	16	Breast milk	4 hours 6 times a day	45 c.c.	23 min.	1 hr., 15 min.	Wt. 1,535 gm.
Fre.	21	Breast milk	4 hours 6 times a day	65 c.c.	2 hours	2 hr., 20 min.	Wt. 1,710 gm.

B. FULL TERM NEW-BORN INFANTS

Name	Age, Days	Food	Feeding Interval	Quantity at Feeding	Interval Before Tracing	Time for Development of First Hunger Period	Remarks
H.	8	Breast milk	4 hours 5 times a day	?	1 hr., 22 min.	3 hr., 50 min.	Wt. 3,590 gm.; gain in 4 days, 90 gm.
Dav.	8	Breast milk	3 hours 8 times a day	75 gm.	1 hr., 55 min.	2 hr., 25 min.	Wt. 4,160 gm.; gain in 5 days 260 gm.; 10 c.c. of milk clot removed from stomach 1 hr. after beginning of hunger contractions
Dav.	9	Breast milk	4 hours (for preceding 24 hours) 5 times a day	?	2 hr., 30 min.	2 hr., 30 min.	Wt. 4,200 gm.; gain in 6 days, 300 gm.; ½ c.c. thick mucus removed from stomach ½ hr. after beginning of hunger contractions
Wes.	8	Breast milk	4 hours 5 times a day	100 gm.	1 hr., 30 min.	3 hr., 10 min.	14 hours fast previous to last feeding
A.	9	Breast milk + cow's milk } aa 8% lactose }	3 hours 8 times a day	70 gm.	1 hr., 45 min.	2 hr., 10 min.	Wt. 3,610 gm.; gain in 6 days 230 gm.; 20 c.c. of thick soft milk clot removed from stomach 50 min. after beginning of hunger contractions
A.	10	Breast milk + cow's milk } aa 8% lactose }	....	70 gm.	1 hr., 52 min.	2 hours	15 c.c. of fluid and curds removed from stomach 30 min. after beginning of hunger contractions
Wal.	10	Breast milk	4 hours 5 times a day	95 gm.	1 hr., 30 min.	4 hours	Wt. 3,240 gm.; gain in 6 days, 260 gm.
D.	12	Breast milk	4 hours 5 times a day	115 gm.	2 hr., 30 min.	2 hr., 30 min.	Wt. 3,720 gm.; gain in 7 days, 400 gm.

C. NORMAL INFANTS OVER TWO WEEKS OF AGE

Name	Age, Days	Food	Feeding Interval	Quantity at Feeding	Interval Before Tracing	Time for Development of First Hunger Period	Remarks
Gor.	18	Breast milk	4 hours 5 times a day	85 gm.	2 hr., 23 min.	4 hours	Wt. 3,500 gm.; gain in 13 days, 70 gm.
Gor.	19	Breast milk	4 hours 5 times a day	110 gm.	1 hr., 58 min.	3 hr., 25 min.	
Way.	Mos. 3.5	Buttermilk + flour + saccharose	4 hours 5 times a day	150 c.c.	2 hr., 27 min.	3 hr., 12 min.	Wt. 4,960 gm.; gain in 7 days, 440 gm.
Way.	3.5	Buttermilk + flour + saccharose	4 hours 5 times a day	150 c.c.	57 min.	3 hr., 20 min.	40 c.c. of thick white materal removed from stomach 20 min. after beginning of contraction period
Way.	3.5	Buttermilk + flour + saccharose	4 hours 5 times a day	150 c.c.	2 hr., 3 min.	4 hr., 35 min.	
Herm.	4	Breast milk	2 or 3 hours irregular	?	2 hr., 45 min.	3 hr., 30 min.	Well nourished; gaining in weight; normal baby; cared for at home; not in hospital
J.	4	Breast milk	5 times a day	?	2 hr., 15 min.	3 hr., 30 min.	Well nourished; gaining in weight; normal baby; cared for at home; not in hospital
Ad.	4	Malt soup	4 hours 5 times a day	125 c.c.	2 hr., 37 min.	3 hr., 30 min.	Wt. 3,500 gm.; gain in 2 weeks, 200 gm.; prematurely born; 1,600 gm. at birth

The time required for the development of hunger in the premature infant is noticeably short. In the case of the full term new-borns the figures obtained agree fairly well with those given by Ginsburg, Tumpowsky and Carlson, but are definitely greater than those obtained by me (mentioned in a preceding paragraph) from infants whose food intake was not accurately known.

The time required for the development of hunger in any one infant is fairly constant over a short period of time, provided the amount and kind of food is not changed. This conclusion rests not only on the results shown in Table 1, but on a dozen other observations on infants whose feeding conditions remained constant during the time in which studies were made.

With the older infants difficulty in maintaining quiet, after the insertion of tube and balloon, limits the number of observations which give positive evidence as to the first appearance of hunger contractions. Many less successful observations on healthy, normally developing infants yield this negative evidence that in such infants more than a month old I did not observe the development of hunger before the end of three hours.

It should be noted further that the contraction period, the first appearance of which is recorded in Table 1, is the first one to develop after feeding. This period is usually short and is not made up of forceful contractions. With Infants J. and A. more intense and more nearly continuous contractions did not begin for four and four and a half hours, respectively.

Habits as to feeding interval affect the time required for the development of hunger chiefly as they influence the emptying time of the stomach. It has been shown that the speed of gastric emptying is proportional to the length of time during which the individual has been without food (Tobler, Haudek and Stigler), and that large feedings are emptied with relatively greater rapidity than small ones (Tobler and Bogen). Habits undoubtedly exert a more powerful influence on the mental factors associated with appetite than on hunger itself.

Tables 2, 3 and 4 illustrate the shorter time required for the development of hunger in infants with chronic nourishment disturbance, and indicate that the presence of hunger contractions is not in itself evidence that the stomach is ready for food.

In the columns headed "Remarks" in Tables 1, 2, 3 and 4, there are notes as to material recovered with the stomach tube after the onset of gastric hunger contractions. In normal babies, however, there probably does exist a relation between the emptying time of the stomach and the interval for the development of hunger.

Observations on the emptying time in infants, so far reported, have been made either with the relatively stiff catheter, the stomach tube,

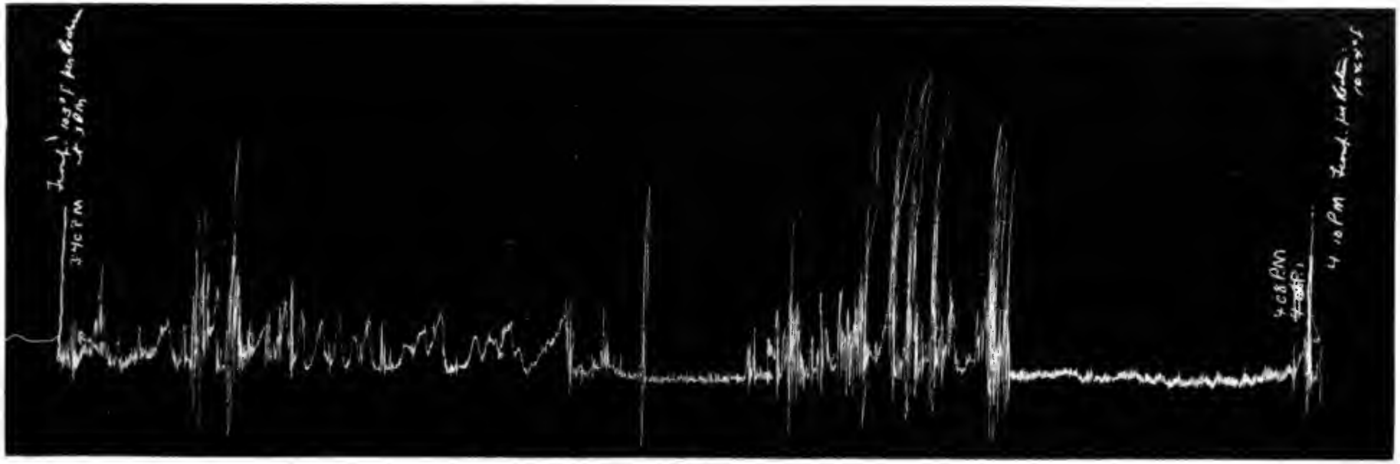

Fig. 8.—N. N., a 2-year-old boy with typhoid fever. Hunger contractions present when rectal temperature ranges between 104.4 and 105 F.

or the Roentgen ray. The flexible tube introduced by Rehfuss should replace the catheter for this purpose; it was used in my work. The literature contains no reports of the time required for gastric digestion in the premature infant. The emptying time in normal breast-fed infants under 1 week is usually less than one hour (Leo). The Roentgen-ray observations of Ladd and of Tobler and Bogen would indicate that in normal breast-fed infants the stomach is frequently not empty until after two to three hours. The figures obtained with the use of the stomach tube by Epstein, Czerny, Keller and Cassel indicate a delayed emptying time in gastro-intestinal disease.

TABLE 2.—Hunger in Atrophy Resulting from Continued Starvation

N. N., aged 2 years; gastric fistula; weight fluctuating between 6,800 gm. and 7,200 gm.; typhoid fever Dec. 1 until Dec. 14, 1916.

Date 1916	Food	Time of Last Feeding	Beginning of Ttracing	
10/19	Diluted cow's milk + general diet	6 a. m.	10:15 a. m.	Practically continuous hunger periods until 10:50 a. m.
10/20	Diluted cow's milk + general diet	10 a. m.	2:12 p. m.	Practically continuous hunger periods until 3:15 p. m.
11/ 1	....	10 a. m.	2:16 p. m.	One hunger period at 2:45 p. m. to 2:50 p. m. Hunger contractions practically continuous after 3 p. m. until 4:50 p. m.
11/10	160 c.c. cow's milk at preceding feeding	2 p. m.	2:45 p. m.	Observations continued until 5:10 p. m. No hunger periods, but child cried or was restless over half of the time
10/11	160 c.c. cow's milk at preceding feeding	2 p. m.	9:00 p. m.	Practically continuous contractions until 11 p. m.
11/11	200 c.c. protein milk + 7% dextrimaltose	5 p. m.	10:12 p. m.	Practically continuous contractions until 11 p. m.
11/12	200 c.c. protein milk + 7% dextrimaltose	5 p. m.	8:41 p. m.	First hunger period at 9:30; practically continuous from 9:45 on until 10:44 p. m.
11/29	200 c.c. protein milk + 7% dextrimaltose	1 p. m.	4:02 p. m.	First hunger period began at 4:35 p. m.; practically continuous from 5 p. m. on until 5:42 p. m.
12/27	200 c.c. protein milk + 7% dextrimaltose + cereals	9 a. m.	12:34 p. m.	Hunger periods practically continuous until 1:30 p. m.
12/28	200 c.c. protein milk + 7% dextrimaltose + cereals	9 a. m.	12:22 p. m.	Hunger periods began about 12:50; hunger periods became continuous after 1:20 p. m.
12/30	200 c.c. protein milk + 7% dextrimaltose + cereals	5 a. m.	10:13 a. m.	Practically continuous hunger periods until 11:20 a. m.

Major, using the Roentgen ray, finds the emptying time delayed in dyspepsia, but accelerated in decomposition. With the same method Pisek and LeWald found the emptying time to be shorter in infants with chronic disturbances of nutrition.

These last findings, taken in conjunction with the already quoted reports of Tobler, and of Haudek and Stigler, that the emptying time is shortened by hunger, are suggestive of the results here obtained experimentally; that is, the greater gastric hunger contraction in infants with chronic nourishment disturbance.

Not only is the interval for development of hunger shorter in such infants, but the contractions become much more intense. Nov. 10,

Fig. 9.—N. N., 2 years old. Tracing shows inhibition from sugar in the mouth; absence of inhibition from quinin in the mouth.

1916, the 2-year-old boy (Table 2), whose weight in spite of a calorically sufficient intake had remained stationary, and whose temperature had been irregular, developed fever and diarrhea. After eight hours of starvation, with temperature normal, the graphic record of his gastric activities resembled those of the starving pigeon and of the premature infant already mentioned. The contractions were continuous and required only twelve seconds for their completion. Next day the child was put on protein milk and thereafter improved.

It is generally agreed that mixtures with high fat content leave the stomach most slowly, while those with low fat and high carbohydrate

TABLE 3.—HUNGER IN EXUDATIVE DIATHESIS

Aus., 7 weeks old, Dec. 19, 1916. Feeding interval 4 hours, 5 times a day.

Date	Weight, Gm.	Food: Breast Milk + Buttermilk + Flour + Saccharose, C.c.	Time of Last Feeding	Beginning of Tracing	
12/19/16	4,450	100	1 p. m.	3:28 p. m.	Hunger contractions began at 3:30 p. m. Hunger contractions continuous from 3:55 to 4:37 p. m.
12/22/16	4,460	100	9 a. m.	11:49 a. m.	Hunger contractions present at 11:49 a. m. Hunger contractions continuous until 12:50 p. m.
12/22/16	4,460	150	1:15 p. m.	3:34 p. m.	Hunger contractions began at 5:45 p. m.
1/ 6/17	4,640	125	8 a. m.	10:55 a. m.	Hunger contractions began at 10:55 a. m. Hunger contractions continuous until 12:21 p. m.
1/ 8/17	4,640	125	8:40 a. m.	11:51 a. m.	Hunger contractions began at 12 m. Hunger contractions strong and continuous after 12:18. Babe was restless
1/11/17	4,650	125	8:45 a. m.	11:11 a. m.	Hunger contractions present by 11:45 a. m. Hunger contractions continuous until 1:35 p. m.
1/13/17	4,740	150	8:20 a. m.	11:03 a. m.	Hunger contractions began at 11:45 a. m. Hunger contractions continuous from 12 to 1 p. m.
1/15/17	4,770	150	8:45 a. m.	11:01 a. m.	Hunger contractions present at 11:20 a. m. Hunger contractions continuout from 11:30 a. m. until 12:50 p. m.
1/15/17	4,770	150	12:50 p. m.	3:21 p. m.	Babe cried a large part of time; no evidence of hunger periods until 5 p. m.

leave most rapidly. In Infants A. and W. the time interval for the development of hunger contractions was much longer when they received low fat and high carbohydrate, and shorter when they received high fat and low carbohydrate. This would be paradoxical if the gastric hunger contractions depended exclusively on the emptying time.

It is, then, only in normal babies, receiving well tolerated food in sufficient quantity, that the development of hunger waits on the emptying of the stomach.

The interval necessary for the development of hunger depends in part on the form of nourishment and is shortest with that food which least satisfies the infant's tissue need (Table 4). The question as to whether the rapid development of hunger in qualitatively poorly

Fig. 10.—Same child as in Figure 9. The tracing shows continuous short contractions in atrophy; after eight hours of starvation.

nourished infants depends on the administration of food deficient in carbohydrate in particular, or on the giving of food poorly tolerated in general, is not answered. Records of the gastric contractions in infants suffering from the chronic nourishment disturbance due to long continued carbohydrate overfeeding (the "Mehlnährschaden" of Czerny) would help to settle this point.

TABLE 4.—Interval for Development of Hunger in Infants with Chronic Disturbance of Nutrition and Showing Influence of Change in Form of Nourishment

Name and Date	Age, Mo.	Diagnosis	Weight, Gm.	Food	Interval Before Tracing	Time for Development of First Hunger Period	Remarks
Til.	3	Atrophy............	Stationary 4,080	120 gm. protein milk + 7% dextrimaltose 5 times a day	....	....	Hunger periods with partial tetanus less than 3 hours after feeding
Ad. 2/26/17	4	Chronic alimentary disorder due to overfeeding with milk	3,300	150 c.c. ½ milk + 10% saccharose 5 times a day	....	....	Hunger contractions present in 2 hours and 20 minutes
Ad. 3/ 8/17	4	Chronic alimentary disorder due to overfeeding with milk	3,500	125 c.c. malt soup 5 times a day	....	....	Babe improved clinically; hunger contractions first appear in 3½ hrs.
Way.	3	Chronic nourishment disturbance with eczema	....	Mixture containing 8% fat. Feeding intervals short and irregular. After entrance to hospital fed 5 times a day	....	....	Entered hospital April 14, 1917
4/14/17	..	....	4,200	150 c.c. ½ cow's milk + 10% saccharose	2 hr., 7 min.	2 hr., 7 min.	Stomach emptied 3 hours after feeding; ½ c.c. of mucus and thick curd obtained
4/23/17	..	....	4,510	150 c.c. ½ cow's milk + 10% saccharose	2 hr., 10 min.	2 hr., 10 min.	Eczema increased; 40 c.c. of clotted milk and clear thin fluid recovered from stomach 3 hours and 25 minutes after feeding
5/ 1/17	..	....	4,960	150 c.c. buttermilk + flour + saccharose	2 hr., 3 min.	4 hr., 35 min.	Eczema has disappeared
5/ 2/17	..	....	4,960	150 c.c. buttermilk + flour + saccharose	2 hr., 27 min.	3 hr., 12 min.	
5/ 3/17	..	....	4,960	150 c.c. buttermilk + flour + saccharose	57 min.	3 hr., 20 min.	40 c.c. of thick white material removed from stomach 20 minutes after beginning of first contraction period

Attention has already been called to the heightened electrical reactions found by Zybell in hungry infants. I also wish to mention the findings of Finklestein, Thiemich and Japha that the electrical irritability is frequently heightened in artificially fed infants, and of Czerny and Moser that there is an increase in the electrical irritability of infants suffering with "Mehlnährschaden." It is possible that the heightened electrical irritability in all depends on the increased hunger contractions due again in part to the constant chemical stimulation reaching the stomach from the semistarved tissues.

Most premature infants and many young infants nurse poorly. The consequent effect on lactation and on the babe's nourishment is serious. An extensive literature on this subject has been developed in German, but there is surprisingly little in French and in English.

In 1888 Auerbach described the infantile manner of sucking, which depends on the chewing muscles, and Escherich showed its teleologic importance. The reflex paths and center in the medulla were demonstrated in 1894 (Basch). Cramer, Suszwein, Finklestein, Rott, Rosenstern, Barth and Kasahara have further studied the question and report results which in general support the theory that the inability to nurse well is to be attributed primarily to an imperfect nervous mechanism and not to muscular weakness.

For further elucidation of the question, tracings of the movements of the empty stomach were taken in two infants who were extreme examples.

The first baby (Baby M.), weighing 2,700 gm. at birth and presenting no anatomic peculiarities, took very little from the mother's breast during the first three weeks, although sufficient milk was expressed therefrom to feed the baby and to complement the feedings of other babies.

The second infant (Baby T.), aged 3 months, had weaned himself from the breast, had developed dyspepsia and atrophy on artificial feeding, and could be made to take his food from the bottle only with great difficulty. He seemed able to fix his attention on anything other than the act of feeding.

In these infants as well as in the five prematures, and in one typical case of congenital myxedema, hunger contractions of at least normal force and duration were present. At the time they were studied, none of the infants was able to nurse successfully. In all, the sucking reflex was qualitatively present.

This study does not solve the problem as to the causation of feeble nursing, but does limit the field of possibilities by excluding derangements of the primitive hunger apparatus.

Carlson reports Rupp's finding that hunger contractions persist during the fever excited by the administration of typhoid vaccine. The boy with the gastric fistula contracted typhoid fever from a carrier. Tracings taken while his rectal temperature ranged between 104.4 F. and 105 F., show the presence of hunger contractions.

Carlson and Ginsburg found hypertonicity and hypermotility in the stomachs of two infants with pylorospasm and stenosis. From a six weeks' old infant (Baby S.) with pyloric stenosis, I obtained records which agree with Carlson and Ginsburg's description of periods of tetanus lasting several minutes interspersed with vigorous contractions of normal duration.

Carlson suggests that pylorospasm and stenosis may be an expression of gastric hypermotility. His cases were seen late, as was the one here reported. In the absence of tracings taken at the beginning of the disease, it is likely that the hypermotility results from the inanition following the obstruction at the pylorus. And without definite knowledge that the stomach was washed empty, the long periods of tetanus observed may represent the so-called visible gastric peristalsis.

SUMMARY

The study of fifty-six infants from birth to 2 years of age gives the following results:

1. Confirmation of previous work, that hunger contractions are greater in the new-born infant, with description of these contractions.

2. Determination of the still greater hunger contraction in the stomachs of prematurely born infants, with description of these contractions.

3. There is no relation between cyanosis and hunger contractions.

4. Inhibition of the hunger contractions from the mouth does not occur in young infants.

5. Inhibition of the hunger contractions from the mouth in older infants is present only as the result of stimuli, which the babe has learned to recognize as food. It does not occur with substances producing equally strong sensory impressions, but which are not considered by the infant as food.

6. Inhibition from the mouth is psychic in character.

7. Reflex inhibition from the presence of food in the stomach is present in infants of all ages.

8. This reflex inhibition from the stomach may be only partially developed in young infants.

9. Successive automatic sucking movements — each sucking act serving as the stimulus for its successor — are present during the hunger state, when the reflex threshold is kept almost constantly low by a rapid succession of hunger contractions.

10. In normally developing breast fed babes, hunger is not ordinarily an immediate cause of crying.

11. The average time required for the development of hunger in healthy infants gaining in weight and receiving a known sufficient amount of food is, in prematures, under one month, one hour and forty minutes, with a maximum of two hours and twenty minutes and a minimum of forty minutes; in full term infants under two weeks, two hours and fifty minutes, with a maximum of four hours and a minimum of two hours; in infants from two weeks to four months,

three hours and forty minutes, with a maximum of four hours and thirty-five minutes and a minimum of three hours and twelve minutes (Table 1).

12. The time required for the development of hunger in any one infant is fairly constant over a short period of time provided the amount and kind of food is not changed (Tables 1, 2, 3 and 4).

13. The time required for the development of hunger in infants with chronic nourishment disturbance is shorter than in normal infants (Tables 2, 3 and 4).

14. The time required for the development of hunger is shorter when the infant receives food which is poorly tolerated (Table 4).

15. Hunger contractions occur in these infants long before the stomach has emptied. Consequently their presence is not in itself an indication that the stomach is ready for food.

16. The feeble nursing exhibited by most prematures and by many older infants is not due to derangement of the primitive hunger apparatus. Hunger contractions are present and of normal intensity in such infants.

17. Hunger contractions were present in one infant with congenital myxedema.

18. Hunger contractions were present in a 2-year-old boy with typhoid fever when the rectal temperature ranged between 104.4 F. and 105 F.

19. Confirmation of previous findings of increased hunger contractions in infants with pyloric stenosis.

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HUNGER AND APPETITE SECRETION OF GASTRIC JUICE IN INFANTS' STOMACHS *

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There is apparently a gastric element in appetite. The contractions of the stomach institute hunger. Its profuse and rich secretion causes an entirely different sensation — not painful, but pleasant. Carlson concludes that the appetite or psychic gastric juice described by Pawlow[1] stimulates sensory nerve endings in the gastric mucosa. The resulting sensation resembles that which follows the first few mouthfuls of good food at a meal to which one has come hungry, and directs the flow of consciousness toward the matter of taking food.

Pediatric literature contains many references to this secretion. Bauer and Deutsch found no gastric juice in the baby's stomach after it had reached eagerly for its bottle. Pfaundler noted that in babes who nursed actively the stomach emptied sooner, and the degree of acidity attained was higher than in babes who were fed passively or through the tube. Cohnheim and Soetbeer, working with gastrotomized new-born pups, obtained juice containing hydrochloric acid even when the pups nursed on nonlactating breasts. A. H. Meyer found a great variation in gastric acidities in the same child and conjectured that the variations might depend on the presence or absence of Pawlow's appetite juice. Schmidt writes that the infant on the breast works and stimulates the secretion of gastric juice. Meisl advocates the use of a pacifier before meals to cause the flow of appetite juice. Bogen, whose material included a 3½-year-old boy with a stenosed esophagus and gastric fistula, concludes that psychic secretion of gastric juice does occur. Nothmann, in 1909, formally investigated the question of the secretion of appetite juice by the infant's stomach, and concluded that it took place even immediately after birth. Rosenstern advised the use of pepsin and hydrochloric acid to stimulate the appetite of infants who nurse poorly. Bönniger could find in pups no relation between the kind of food and the secretion of gastric juice.

With the exceptions of the work done on pups, and Bogen's work on a 3½-year-old boy, the foregoing is all brought into question because it relies on the use of the ordinary catheter or stiff stomach tube, which

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1. References to the literature will be found at the end of the article.

does not permit accurate quantitative studies. A still more serious criticism, and one which leaves the whole subject open, is that in none of the quoted work is the possibility of a continuous secretion of gastric juice sufficiently taken into account.

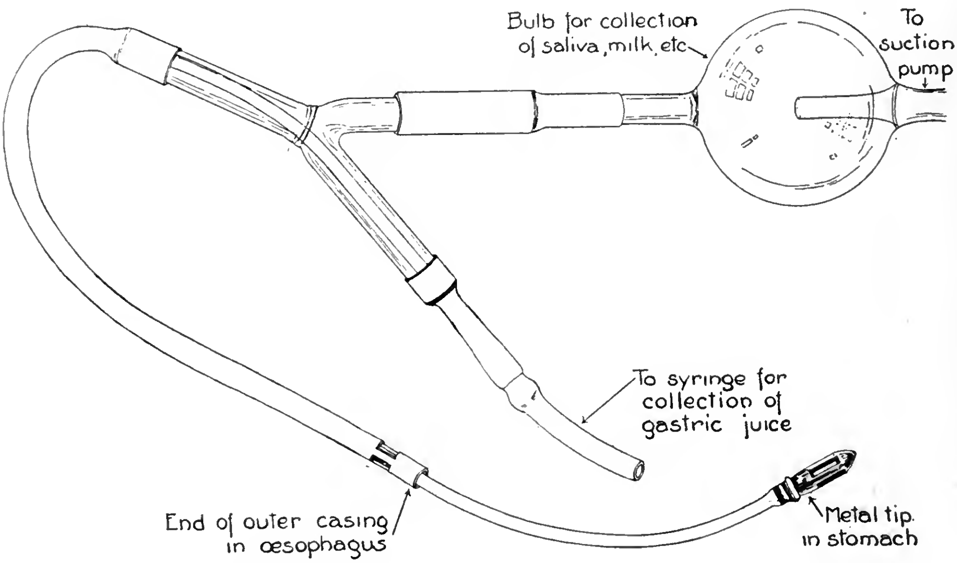
In 1888 Leo found free hydrochloric acid in the stomachs of unfed new-born babes, and noted that in older infants the stomach was rarely entirely empty, so that he could usually recover a few drops of thick, yellowish acid fluid. He washed out the stomach and again inserted the tube and then obtained only wash water from the preceding washings. Consequently Leo concluded that the acid juice obtained by him from the "empty" stomach was the gastric juice remaining from the last meal, concentrated by the absorption of water. Wohlmann reported that the secretion of the infant's empty stomach is viscid, colorless, glassy, and without free hydrochloric acid. Wohlmann took his specimens from one to two hours after feeding. The teachings of Pawlow that gastric secretion depends on appetite or on food or other stimuli in the stomach impressed the medical mind so deeply that until the present decade all gastric secretion was interpreted in the light of his investigations. A. H. Meyer concluded that the passage of the stomach tube does not excite the secretion of acid gastric juice. Pawlow's published work supports the same conclusion. Engel reports a 4-week-old babe with pyloric stenosis and a jejunal fistula. From this infant, who was fed through the fistula, Engel obtained by way of the esophagus from 60 to 200 c.c. of gastric juice daily. The total acidity of this juice ranged from 60 to 70 and was nearly entirely made up of free hydrochloric acid. Engel was unable to explain his findings except on the basis of a pathologic hypersecretion, which he thought might have caused the pyloric stenosis. Alfred F. Hess, in 1913, showed that the stomach of the unfed new-born babe secretes a highly acid juice, and he concluded further that saliva does not act as a stimulus to the production of such juice. He was unable to determine a relationship between the amount of sucking and the amount of juice secreted. Sedgwick recovered acid stomach and duodenal contents three and four hours after nursing. In 1905 Boldyreff reported continuous secretion of the gastric glands in starving dogs. Ten years later Fowler, Rehfuss and Hawk concluded that, in man, the gastric glands are never idle, while Carlson demonstrated the continuous secretion of gastric juice in the empty stomach of normal adults. Referring to its secretion during the hunger state, Carlson calls it hunger juice.

It is evident that the determination of the secretion of an appetite juice in the infant's stomach must be made in conjunction with the determination of its continuous secretion.

The flexible tube with the slotted weight at the tip described by Rehfuss, combined with any simple syringe for gentle aspiration, makes

an excellent instrument for the study of the physiology of the stomach of the infant. A smaller tip can be made for those infants who cannot swallow the ordinary tip. With this apparatus I have repeatedly recovered from the infant's stomach the entire 30 to 50 c.c. of water introduced into it and never have lost more than 2 c.c. in the washing. Furthermore, large, thick, gelatinous clumps of mucus and curd are removed without difficulty.

In order to avoid, as far as possible, contaminating the gastric juice with saliva, and to permit the carrying out of sham feeding, I converted a No. 21 F. soft rubber catheter into an outer casing for the Rehfuss tube. When in place this outer casing terminates internally in the esophagus, and externally with a suction apparatus. The whole is explained in the accompanying illustration, which is one-half actual size.



Author's apparatus for removing gastric contents from infants; one-half actual size.

The experimental procedure was as follows: If the babe fasted all night, he was given water at 5 a. m. in quantity equivalent to his usual feeding. When the stomach was examined a few hours later, milk remains were never found. If the period without food were shorter, his stomach was thoroughly washed out and observations begun an hour later.

If no aspiration is applied to the stomach tube during the half hour, the amount obtained is usually less than 1 c.c. The usual procedure was to insert the tube, exert suction to empty the stomach of any content, then allow the tube to remain one-half hour without suction, and

collect the specimen, if any. Repeat the procedure, exerting gentle suction every two and one-half minutes and collect the specimen. Exert suction in the same way during a third half hour while the sham feeding progresses. The final two specimens only are listed in the accompanying table.

As a rule, no secretion was obtained for five minutes after the insertion of the tube. On one occasion gastric juice containing free hydrochloric acid was obtained within two minutes of the time at which introduction of the tube began (Baby A.). This is less than the latent time usually required by the gastric glands (Carlson, Pawlow) and is further evidence that the secretion here obtained was not produced artificially by the apparatus.

To stimulate an appetite secretion, the babe was given a pacifier threaded over the tube, or, the food to which he was accustomed was administered by a medicine dropper, or, with the artificially fed babes, from their usual nursing bottle. The infant always sucked vigorously during this procedure. If the babe sucked before sham feeding began, it has been noted in the table. As a rule, the babes slept or were quiet and did not suck, except after the beginning of the sham feeding. The presence of the tube seemed to discommode these babes very little. There certainly was no psychic excitement to depress the action of the gastric glands while the babes were smacking and sucking over their food.

In three cases only, as noted in the table, did food reach the stomach. Strictly speaking, neither these instances nor the specimens which contained blood should be considered as offering evidence on either the subject of "hunger" or "appetite" gastric juice. The only demonstrable effect of the blood, which was never present in more than a trace, was to lower the acid titration values. On the three occasions on which milk reached the stomach, larger amounts of secretion was obtained.

The titrations were done against tenth-normal sodium hydroxid, using di-methyl-amino-azobenzol and phenolphthalein as indicators. The hydrogen-ion concentrations were done by the gas chain method. I wish to thank Dr. J. F. McClendon for his courtesy in allowing the use of his apparatus.

The "appetite" gastric juice is characterized by its relatively profuse secretion and high acidity. Neither characteristic was present in the juice obtained after sham feeding in these infants. On the contrary, the juice obtained differed little in character and quantity from that obtained before sham feeding was begun.

It will be seen that the empty stomach of the infant continuously secretes a juice which at times is as acid as that of the adult, and that the infant's stomach does not secrete an "appetite" or psychic juice.

TABLE 1.—Comparative Secretion of Hunger and Appetite. Gastric Juice

Name	Age	Length of Preceding Starvation, Hours	Behavior During Collection of Continuous Secretion or "Hunger" Juice	Amount of "Hunger" Juice per ½ Hour, C.c.	Description of "Hunger" Juice	Method of Provoking Appetite Juice	Amount of Appetite Juice per ½ Hour, C.c.	Description of Appetite Juice
Ow.	15 hrs.	Unfed	Cried some; slept most of time	0.9	Slightly viscid; trace of saliva; no blood; translucent; free HCl 0; total acid 4			
Wal.	7 days	4	Slept................	3.0	Thick, viscid trace of saliva; free HCl 8; total acid 18	Sucking on pacifier..........	3.0	Thick, viscid, trace of saliva; free HCl 2; total acid 18
Wal.	9 days	6	Quiet; no sucking...	3.0	Trace of saliva; free HCl 2.5; total acid 17.5			
Wes.	2 hrs.	Unfed	No sucking..........	6.0	CH+ = 0.3 × 10^{-2}; free HCl 50; total acid 60			
Wes.	7 days	13	No sucking..........	1.75	Yellowish, clear, viscid; Gmelin test neg.; free HCl 18; total acid 39			
He.	6 days	11	Slept throughout; sucked a little	1.0	Slightly viscid; no saliva; no blood; free HCl 5; total acid 40			
P.	9 days	12	Slept; no sucking...	1.0	Viscid, clear, no foam; trace of blood; free HCl neg.; total acid 30	Sham feeding: 5 c.c. breast milk; sucked vigorously for 15 minutes	0.5	Thick, viscid, trace of blood; free HCl 0; total acid 30
A.	11 days	12	Slept most of time; no sucking	1.5	Slightly viscid trace of blood; free HCl 60; total acid 80	8 c.c. breast milk; sucked vigorously for 20 minutes	2.5	Brownish, blood stained, slightly viscid; free HCl 54; total acid 60
S.	12 days	13	Cried; no sucking...	2.0	Transparent, slightly viscid; free HCl 55; total acid 75	5 c.c. breast milk; sucked vigorously for 15 minutes	1.0	Thin, transparent, slightly viscid; free HCl 60; total acid 80
H.	17 days	13	Slept most of time; sucked occasionally	2.0	Clear, slightly viscid; trace of blood; free HCl 30; total acid 60	10 c.c. breast milk; sucked on tube	1.0	Clear trace of blood; free HCl 10; total acid 40
K.	3.5 mos.	17	Sucked on tube......	3.5	Translucent viscid; trace of saliva; free HCl 7; total acid 28	5 c.c. cow's milk + saccharose; sucked	10.0	Clear, viscid, trace of saliva; small amount of milk; free HCl 0
K.	3.5 mos.	17	Sucked constantly	3.0	Trace of saliva; free HCl 33; total acid 38	Cow's milk + saccharose; sucked	2.0	Total acid 24; turbid, blood stained; free HCl 25; total acid 55
Ad.	5 mos.	16	Slept; no sucking...	3.0	Clear viscid, trace of saliva; free HCl 56; total acid 70	Malt soup	8.0	Contained milk; free HCl 18; total acid 45
Ad.	5 mos.	17	Slept; no sucking...	3.0	Thin, clear, slightly greenish; free MCl 80; total acid 110; CH+ = 0.5 × 10^{-1}	15 c.c. malt soup; sucked vigorously 20 minutes	5.0	Contains 0.5 c.c. milk clot; free HCl 10; total acid 45; CH+ = 2 × 10^{-1}
Wi.	7 days	25	Cried much; did not suck	1.0	Thick, viscid trace of blood; free HCl 10; total acid 40	Sham feeding: 10 c.c. breast milk; sucked vigorously; quiet	0.2	Clear mucus; free HCl 0
Ca.	9 days	24	Slept throughout; did not suck	3.0	Turbid, viscid fluid containing trace of blood; free HCl 12; total acid 32	Sham feeding: 10 c.c. breast milk; sucked vigorously; did not cry	0.9	Turbid, viscid, containing partially digested blood; free HCl 22; total acid 55
Ni.	11 days	23	Cried ⅓ of time; sucked a little	1.5	Viscid mucus; free HCl 0; total acid 8	Sham feeding: 10 c.c. breast milk; sucked vigorously; cried a little	1.0	Turbid, viscid, mucus; free HCl 0; total acid 10
P.	1 mo.	25	Slept ½ of time; cried a good deal; no sucking	1.8	Trace of saliva; viscid; free HCl +; total acid 9	Sham feeding: 10 c.c. breast milk; sucked some; cried much	1.0	Viscid mucus; trace of blood; free HCl 10; total acid 16
Wa.	5 mo.	21	Slept most of time; sucked a little	8.0	Clear, slightly viscid; free HCl 72; total acid 90	Sham feeding: 10 c.c. malt soup; sucked vigorously; whined and teased	14.0	Slightly viscid, cloudy; small amount of blood-stained mucus; free HCl 60; total acid 80

This accords with the absence of psychic inhibition of the hunger contractions.

As indicated by the digestion of egg white in Mett's tube, the infant's hunger juice contains pepsin.

Reiche has demonstrated the absence of a duodenal reflux into the infant's stomach. The present findings support his conclusion. What, then, becomes of this continuous secretion under circumstances such as enforced therapeutic starvation from twenty-four to forty-eight hours? Pfaundler has conjectured that at the close of digestion the alkaline secretion of the pyloric glands gradually neutralizes the acid content of the stomach. I cannot support this view. The finding of a greater quantity of juice when a more continuous suction is maintained, the frequent absence of juice when the tube is first inserted, and Sedgwick's finding that the young infant's duodenal contents are acid, favor the conclusion that at least a portion of this juice makes its way into the intestine.

It seems probable, therefore, that the secretion of the alkaline pancreatic and intestinal juices, which in the adult regurgitate into the stomach, as demonstrated by Boldyreff, and lower the acidity of the juice in the stomach (Carlson, Rehfuss and Hawk and Boldyreff), is, in the infant, relatively deficient.

The hunger juice is delivered through the tube intermittently. The most profuse secretion is, as a rule, associated with the higher acidities; this is also true in the adult (Carlson). The largest amounts were obtained from one of the unfed new-born babes and from the older infants. It is readily seen that the stomach of the starving infant can secrete from 50 to 200 c.c., or more, of highly acid juice daily. This equals the amount Engel obtained from his case of pyloric stenosis, which has served as the clinical basis for the theory that hyperacidity or hypersecretion of the gastric juice is an etiologic factor in that disease.

Furthermore, this demonstration of the capacity of the infant's stomach to secrete a highly acid juice, makes it probable that the low acid values found during gastric digestion of milk are in part due to its binding power for acid (Aron), and in part due to the relatively slight stimulation which it exerts on the gastric glands (Pawlow, Moore and Allanson). Huenekens found a hydrogen ion concentration of 174×10^{-5} in a 9½-months-old infant after a meal of soup and vegetables. Most of his results were lower, however. No such studies have been made in younger infants.

Experience in the clinic of the University of Minnesota and in other clinics (Rott) has proved the advantage which is gained in feeding the premature infant by tube. Theoretical objections to the use of

the tube have been based principally on the assumed existence of an appetite gastric juice (Pfaundler).

The amount of saliva collected during the experiments on gastric secretion was measured in six cases.

W.— 7 days	No sham feeding	7 c.c. in 40 minutes
H.—17 days	Sham feeding	14 c.c. in 2 hours
P.— 1 mo.	Sham feeding	25 c.c. in 1.5 hours
Ne.—11 days	Sham feeding	15 c.c. in 1.5 hours
P.— 9 days	Sham feeding	8 c.c. in 1.5 hours
S.—12 days	Sham feeding	10 c.c. in 1.5 hours

The saliva collected was the thick viscid product of the submaxillary glands, which Schilling has noted as being preponderant during early infancy.

Allaria points out the chemical and mechanical advantages of having the milk well mixed with saliva, and estimates that the infant secretes an amount equal to from 10 to 20 per cent. of the ingested food. The tube-fed infant may do without this secretion in part or altogether, but there is no evidence that his gastric secretion is less than that of the actively nursing babe.

What light does this study throw on deprivation of food as a therapeutic agent? In infancy such a measure finds its chief field in acute alimentary disorders and summer diarrheas. The significant fact is that in hunger the infant's stomach secretes continuously, but with intermittent intensity, a highly acid juice, which at least in part flows into the small intestine where it may play a disinfecting or detoxicating rôle.

SUMMARY

1. Description of an apparatus by which sham feeding can be carried out and gastric juice collected under conditions which give positive evidence of the amount secreted.

2. There is no appetite or psychic secretion of gastric juice in the young infant. This disproves the present view, which is based on insufficient experimental evidence.

3. The empty stomach of the hungry babe secretes a gastric juice which often is as acid as that found in the adult's stomach.

4. The more profuse this secretion, the higher is its acidity. It contains pepsin.

5. This secretion is not neutralized in the stomach, but flows out into the small intestine. Regurgitation through the infant's pylorus does not occur.

6. The theoretical objections to tube feeding in prematures because of the lack of stimulation of an appetite gastric juice are not valid. However, a disadvantage may lie in this: that such feeding precludes the usual admixture of the milk with saliva.

Therapeutic starvation in acute alimentary disorders and in summer diarrheas may owe its success in part to the heightened tonus of the alimentary tract, and in part to the pouring out of highly acid detoxicating and disinfecting gastric juice into the small intestine.

I wish to acknowledge my indebtedness to Dr. J. P. Sedgwick for the use of material from his service in the University of Minnesota Hospital.

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STUDIES IN THE NEPHRITIS OF CHILDREN *

FIRST PAPER

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RENAL FUNCTION TESTS

For many years the study of nephritis has attracted a great deal of attention from clinicians. The problems involved are so complicated and so many, the correlation of different anatomic lesions with variations in functional capacity is so difficult, and the stages through which any given case of nephritis may pass are sometimes so varied in the pictures they present, that it is indeed impossible for anyone to feel that he understands nephritis, no matter how much experience he may have had with it. Up to ten or twelve years ago the problem that chiefly interested investigators was a study of the histologic changes produced in the kidney tissue by different types of nephritis, and little attention was paid to changes in the functional capacity of the organ. At present the reverse is true, and studies in kidney function dominate the literature on nephritis in the last decade. Nearly all the work, however, has been done with adults, and nephritis in children has received comparatively little attention.[1] Two years ago, at the suggestion of Dr. John Lovett Morse, I became interested in nephritis, and since then have studied between sixty and seventy cases of acute and chronic nephritis in the wards of the Children's Hospital.* During the course of these investigations many interesting questions have arisen, which will be discussed later, and the present paper will take up only functional tests.

There is this great difference between nephritis as seen in adults and in children. In adults there may be recognized, broadly speaking, two great groups of nephritic cases; one dependent on acute infectious processes somewhere in the body, the toxins of which injure the kidneys either temporarily or permanently; the other dependent on slow-going degenerative changes in the blood vessels, which produce so-called "chronic interstitial" nephritis, or "cardiorenal" disease. By far the majority of cases of nephritis in adults fall into the second group, and

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1. For a review of the literature dealing with nephritis in children see Hill, L. W.: Boston Med. and Surg. Jour., 1917, **177,** 313.

it is this group of cases which has been most extensively studied. On the other hand, I do not feel that it is too strong to say that nearly all nephritis in children depends on infection; for practical purposes we can rule out the slow-going "vascular" or chronic interstitial type. (A few cases of "chronic interstitial" nephritis in children have been reported, however.) Thus it may be seen at the outset that in dealing with nephritis in children we are dealing with a far different problem from that of nephritis in older persons, and we must not necessarily expect functional tests to show the same phenomena as in the adult.

Many tests of kidney function have been used in the last few years, some of which have passed into oblivion, some of which have survived. These functional tests may be divided into two broad groups, the first of which comprises those tests that measure the power of the kidney to excrete chemical substances not ordinarily contained in the food, or "körper fremden" substances, as the Germans have put it. The second group comprises those tests which measure the ability of the kidney to excrete substances ordinarily contained in the food. Three of the most important functions of the kidney are to excrete nitrogen, salt and water, and it is these, therefore, that are usually taken as the test substances to determine the kidney's functional power.

Phthalein Test.—A number of tests with substances foreign to the body have been proposed, but the only one which has survived is the phenolsulphonephthalein test of Rowntree and Geraghty. This has been found, after extended use all over the world, to be the most practical test of kidney function for general clinical use.

In this test, which is now familiar to everyone, 6 mg. of the dye phenolsulphonephthalein is injected intramuscularly, and all urine passed for two hours is saved. This is made alkaline with sodic hydrate to bring out the color of the phthalein, diluted to 1,000 c.c., and the intensity of the resulting color is compared with that of a standard solution. The result is expressed in per cent. of phthalein excreted in two hours; the test is therefore one of the rapidity of the kidneys to excrete the dye. A normal adult should excrete from 50 to 80 per cent. of the phthalein in two hours, and any figure above 50 is usually considered normal for an adult. The figures for children vary considerably from this, as will be seen.

The results of this test in twenty-seven normal children are shown in Table 1. These children might not perhaps be considered as strictly normal children, inasmuch as they were all in the hospital for various reasons, but they were all free from any condition which could possibly influence the function of the kidney, such as fever, malnutrition, etc. A Duboscq colorimeter was used.

It may then be said that the average phthalein excretion for normal children is somewhere in the neighborhood of 75 per cent., and that if the function is below 60 per cent. it may be considered as abnormal.

These figures agree fairly closely with those of Tileston and Comfort[2] and Leopold and Bernhard,[3] whose average figures for normal children are 78 per cent. to 81 per cent., and 70 per cent., respectively.

The test was performed on thirty-seven children with nephritis of all degrees of severity. Twenty-one cases were acute, sixteen chronic.

The average excretion of the twenty-one acute cases was 59 per cent., or 17 per cent. below the normal average; 59 per cent. would be a normal phthalein excretion for most adults.

The average excretion of the sixteen chronic cases was 63 per cent., or 13 per cent. below the normal average of 76 per cent.

TABLE 1.—Phenolsulphonephthalein Excretion in Normal Children

Age, Years	Phthalein Excretion, Per Cent.	Age, Years	Phthalein Excretion, Per Cent.
2½	64	8	77
5	77	8	79
6	80	9	66
6	71	9	70
7	69	10	80
7	90	10	74
7	77	10	65
7	77	10	100
7	66	10	76
7	66	11	80
7	74	11	77
7	80	11	80
8	87	11	90
8	87		

High, 100 per cent.; low, 64 per cent.; average, 76 per cent.

DISCUSSION

From the figures in Table 2 it can be said that the phthalein excretion is diminished in many cases of acute or of chronic nephritis in children, and that it is likely to be a little lower in the acute cases than it is in the chronic. The reverse is true in adults. Many chronic "cardiorenal" cases show a phthalein excretion of 5 to 10 per cent., or even sometimes such a slight trace that it cannot be read at all. Most cases of chronic nephritis in children are of a mild type, and even the very severe cases, of which we have seen a number, do not show nearly as much interference with phthalein excretion as one would expect. It is no uncommon thing to see a normal excretion in a child who has had nephritis for two or more years, who is edematous and anemic, and who has an increased blood pressure and a urine loaded with albumin and casts. In dealing with children, then, normal or high phthalein excretion helps us very little, as the test may be high in many cases in which there is unquestionably severe kidney damage. A low

2. Am. Jour. Dis. Child., 1915, **10,** 278.
3. Am. Jour. Dis. Child., 1916, **11,** 432.

TABLE 2.—Phenolsulphonephthalein Excretion in Nephritis

Age, Years	Phthalein Excretion, Per Cent.	Remarks
ACUTE CASES		
9	63	Mild
9	62	Severe; bloody urine; blood pressure 140
6	62	Severe; bloody urine
4	80	Edematous; blood pressure 135
10	54	Moderately severe
8	50	Moderately severe; considerable edema
5	66	Moderately severe
10	71*	Severe; much edema
5	76	Moderately severe; slight edema
3	53, 50	Moderately severe; slight edema
4½	66	Mild
5	65	Moderately severe
3	83	Moderately severe
4	30	Moderately severe
5	70	Mild
7	64, 35	Severe; much edema
8	43	Moderately severe
4	43	Moderately severe
4	75	Severe; much edema
4	21	Severe; much edema
5	43	Severe; much edema
CHRONIC CASES		
7	55	Chronic interstitial nephritis; blood pressure 210
9	70	Moderately severe; two years' duration; blood pressure 150
7	66	Mild; one year's duration
9	80	Mild; subacute
2	66	Very severe; much edema; blood pressure 130
12	66	Mild
11	69	Very severe; much edema
7	50, 37, 70	Moderately severe; one year's duration
5	33, 60, 54, 30, 44	Very severe; two years' duration
6	62, 71, 60	Severe
4	87	Mild; subacute
6	50	Moderately severe
13	71	Mild; two years' duration
4	50	Moderately severe
3	60	Moderately severe
8	59	Moderately severe

* After decapsulation.

The average excretion of the twenty-one acute cases was 59 per cent., or 17 per cent. below the normal average; 59 per cent. would be a normal phthalein excretion for most adults.

function, however, tells us a good deal: in acute nephritis it puts us on our guard, and makes us consider the case a severe one whether or not it appears so clinically; in chronic nephritis it tells us that permanent damage has been done to the kidney, and makes us very guarded in our prognosis.

Added Salt and Urea Test.—Another method of testing renal function which has been in vogue is the addition of a known amount of salt and urea to a standard diet, and then determining how much of the

added salt and urea has been excreted in a given period of time. In adults this test is usually performed as follows:[4]

The patient is put on a constant standard diet containing a known amount of nitrogen, salt and water, and the amounts of salt and nitrogen in the urine are quantitated daily until their excretion has become constant. This usually takes from two to three days. On the third or fourth day 10 gm. of salt is added to the diet and by daily urine analyses it is determined how long the kidneys take to excrete the added salt. Normally it should be excreted in two days. After the ability of the kidneys to excrete salt has been determined, 20 gm. of urea is added to the diet, and the rapidity of excretion of this is determined in the same way.

This test necessitates keeping the patient on a carefully fixed diet and collecting accurate twenty-four hour urine specimens for eight or ten days. Any such procedure as this is obviously impossible in the case of small children, owing to refusal to eat, wetting the bed, etc. It was felt desirable to modify this test in dealing with children, and this was done as follows:

For three days the child was kept on the following standard diet;

Oatmeal, 4 tablespoonfuls	1 orange
Bread, 3 slices	1 small baked potato
16 per cent. cream, 4 ounces	Sugar, 4 drams
Salt-free butter, 2 ounces	Water, 34 ounces

Whole milk, 16 ounces

This diet contains about 5.7 gm. of nitrogen. On the third day the twenty-four-hour output of salt and nitrogen in the urine was determined, and the next day 10 gm. of urea (containing 4.65 gm. nitrogen) and 5 gm. of salt were added to the diet. (Given together in a little water, early in the morning.)

The nitrogen and salt were then quantitated in the following twenty-four hour urine specimen, and by subtracting the urinary nitrogen and salt of the previous day the amount of these substances eliminated in the twenty-four hours after the addition was determined. I realize that it is better to give the salt and urea on different days than to give them together, and that there are also other objections to this simplified method of procedure, but even with this simple method many failures resulted, owing to th: capriciousness of the child's appetite, unwillingness to take the salt and urea, wetting the bed, etc., and the cases reported represent only a portion of many attempted.

Twelve cases of nephritis were studied by this method, six of them acute, six chronic.

DISCUSSION

As may be seen from a glance at the table of normals (Table 3), the salt and urea excretion varied normally within rather wide limits, and it is therefore difficult to establish a normal standard. Age seemed to bear no relation to a large or a small excretion. Inasmuch as normal children vary so much in their reaction to this test, it is valuable only within very wide limits, and the excretion of salt and nitrogen may be said to be abnormal only if it is very much impaired. In six of the twelve cases studied the excretion of salt, of urea, or of both, may be said to be abnormally low (those marked †) ; in the rest of the cases it may be said to be normal. Marked impairment of salt excretion

4. Frothingham: Am. Jour. Med. Sc., 1915, **149,** 808.

occurred more frequently than of nitrogen, especially in those cases which were, or had been, edematous.

Value of the Test.—The added salt and urea test may be of some value in indicating that the function of the kidneys is impaired, but only if the excretion is very poor, inasmuch as the normal response to the test may vary within such wide limits. If the excretion of both salt and urea is high, it is safe to assume that the kidney's function is not much impaired, as the test is an extremely severe one, for Zondek[5] has shown that diseased kidneys may be able to eliminate a large amount of urea or of salt *alone,* but not a large amount of both substances when they are ingested together. Even if this test occasionally does yield information of value, it is not at all adapted for general use in children, as the difficulties of carrying it out accurately are well nigh insurmountable.

TABLE 3.—Results of Salt and Urea Test of Renal Function

Age, Years	Salt and Nitrogen Above Control * Salt, Gm.	Nitrogen, Gm.	Remarks
NORMALS			
11½	4.24	3.33	
10	1.47	5.00	
8	2.90	3.60	
10	2.40	3.40	
6	3.16	4.12	
11	4.22	4.32	
6	2.16	3.70	
6	3.78	4.55	
NEPHRITICS			
4	—0.25	1.96	Severe acute nephritis; no edema†
4	2.96	2.80	Mild acute nephritis; slight edema
10	3.84	2.88	Mild acute nephritis; no edema
7	1.90	3.24	Severe acute nephritis; no edema
8	3.90	3.16	Severe acute nephritis; no edema
9	3.80	3.00	Moderately severe acute nephritis; no edema
4	1.37	2.53	Severe chronic nephritis; considerable edema
9	—1.60	—2.86	Severe chronic nephritis; moderate edema†
7	3.02	2.40	Mild chronic nephritis
7	4.88	5.62	Mild subacute nephritis
11	4.22	6.26	Mild chronic nephritis
6	5.45	3.85	Severe chronic nephritis after decapsulation (Edebohls' operation)

* By this is meant the excess of salt and nitrogen excreted on the test day over that of the previous day.

† A minus sign indicates that less salt or urea were excreted on the day after their addition to the diet than on the day before.

Twelve cases of nephritis were studied by this method, six of them acute, six chronic.

5. Zondek: Ztschr. f. klin. Med., 1915, **82,** Nos. 1 and 2.

The "Two Hour" Renal Test.—This test was first proposed by Hedinger and Schlayer[6] in 1914. In this country it has been used extensively by Mosenthal[7] in Baltimore, and O'Hare[8] in Boston. It is performed as follows:

> The patient is put on a full diet, containing a considerable amount of protein, of purin extractives and of salt, in order to make a demand on the power of the kidneys to excrete such a diet. The fluid allowance is fixed, and no fluid is allowed between meals. The noon meal is considerably larger than either of the others and is designed particularly to call forth the kidney's power of excretion. The urine during the test day is collected in two-hourly periods, and the night urine in one sample. The amount and specific gravity of each two hourly specimen is noted as well as the amount and gravity of the night urine. The amount of salt and nitrogen and the salt and nitrogen concentration of each specimen are quantitated.

Mosenthal[7] has well explained the principles of this test as follows:

> The kidney expresses its diminished power to functionate by a fixation of its power of concentration. The normal kidney yields a urine of medium, low or high specific gravity according to the proportion of fluids and solids that must be excreted in order to maintain the composition of the body fluids at a constant level. The diseased kidney, on the other hand, loses this flexibility, and the power to answer the demand for a more concentrated or a more dilute urine no longer exists.

The normal response to a test meal is shown by a considerable variation in the amount, specific gravity, nitrogen and salt concentration of the two-hourly specimens, and by a relatively small amount of night urine, of high (1.020) specific gravity, and high nitrogen concentration (1 per cent.). A kidney whose function is impaired excretes a urine which varies very little in specific gravity and nitrogen and salt concentration in each two-hourly period. The gravity may be fixed at a low or a fairly high level. Also the amount of night urine is likely to be large, and the nitrogen concentration and specific gravity low (below 1 per cent. and 1.020, respectively). The fixation of the specific gravity is the most important point to observe, and it is not at all necessary to make salt or nitrogen determinations on any of the specimens. Moreover, it is not essential that the patient consume the exact diet indicated; it is merely necessary that the diet be a full one, containing a considerable amount of purin bases, nitrogen and salt, and that the noon meal shall contain more of these than the other meals. It is essential that the fluid taken with each meal be the same in amount, and that no fluids be taken between meals or at night. The test takes only one day, does not require the patient to be on a particularly rigid diet, and if, perhaps, one two-hour urine specimen is lost, no particular harm is done. *This, therefore, is a test which is very well adapted for ordinary clinical use, as in its simplest form no long drawn out procedure or complicated urinary analyses are necessary.*

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6. Schlayer: Arch. f. klin. Med., 1914, **114,** 120.
7. Mosenthal: Archives Int. Med., 1915, **16,** 733.
8. O'Hare: The Archives Int. Med., 1916, **17,** 711.

I have modified the original procedure somewhat, especially for use in children, and have carried it out in this manner.

The child is put on the following diet:

Breakfast	Dinner
Cereal, 2 tablespoonfuls	Chopped meat, 2 tablespoonfuls
Bread, 1 slice	1 egg
Butter, ½ square	1 potato
Apple sauce, 2 tablespoonfuls	Butter, 1½ cubes
Milk, 6 ounces	Milk, 6 ounces
Water, 4 ounces	Water, 4 ounces
Extra salt, 1 gm.	Extra salt, 1 gm.
Caffein sodium benzoate, 2 grains	Caffein sodium benzoate, 2 grains

The caffein is given instead of the tea or coffee which is given to adults to secure diuretic response from the kidneys.

The two-hour urine specimens are then collected in the usual manner, starting at 6 in the morning, and continuing until 6 at night. The night urine is collected from 6 p. m. to 6 a. m.

Then the gravity of each two-hourly specimen, and the amount of night urine is measured, a fixation of gravity in each specimen indicating loss of power on the part of the kidney to vary the concentration of solids in the urine, and hence impaired function. The determination of the specific gravity of each specimen is really all that is essential, but in most cases we have measured the day and night urine; and in some the nitrogen concentration of the night urine.

As controls, fifteen normal children were studied, for as far as we know, no work with this test has ever been done with children, and it is desirable to establish a standard of normality.

NORMALS

Time	No. 1 Aged 11 Yrs. Specific Gravity	No. 2 Aged 10 Yrs. Specific Gravity	No. 3 Aged 11 Yrs. Specific Gravity
6- 8	1.018	1.013	1.016
8-10	1.010	1.021	1.022
10-12	1.015	1.023	1.023
12- 2	1.021	1.024	1.020
2- 4	1.017	1.027	1.015
4- 6	1.021	1.028	1.011
6- 6	1.023	1.020	1.020
	Night urine, 260 c.c.	Night urine, 320 c.c.; nitrogen concentration, 88%	Night urine, 165 c.c.; nitrogen concentration, 1.1%

Time	No. 4 Aged 7 Yrs. Specific Gravity	No. 5 Aged 10 Yrs. Specific Gravity	No. 6 Aged 10 Yrs. Specific Gravity
6- 8	1.017	1.016	1.015
8-10	1.025	1.009	1.016
10-12	1.025	1.018	1.022
12- 2	1.022	1.009	1.028
2- 4	1.030	1.025	1.020
4- 6	1.026	1.025	1.025
6- 6	1.032	1.027	1.027
	Night urine, 75 c.c.; nitrogen concentration, 2%	Night urine, 210 c.c.; nitrogen concentration, 1.7%	Night urine, 325 c.c.

Time	No. 7 Aged 6 Yrs. Specific Gravity	No. 8 Aged 9 Yrs. Specific Gravity	No. 9 Aged 10 Yrs. Specific Gravity
6- 8	1.019	1.018	1.017
8-10	1.022	1.018	1.004
10-12	1.027	1.024	1.019
12- 2	1.027	1.028	1.020
2- 4	1.025	1.027	1.023
4- 6	1.028	1.026	1.025
6- 6	1.030	1.025	1.030
	Night urine, 160 c.c.; nitrogen concentration, 2.5%	Night urine, 480 c.c.; nitrogen concentration, 1.10%	Night urine, 120 c.c.

Time	No. 10 Aged 9 Yrs. Specific Gravity	No. 11 Aged 9 Yrs. Specific Gravity	No. 12 Aged 9 Yrs. Specific Gravity
6- 8	1.018	1.022	1.020
8-10	1.017	1.212	1.012
10-12	1.020	1.018	1.009
12- 2	1.015	1.018	1.020
2- 4	1.015	1.014	1.019
4- 6	1.023	1.017	1.016
6- 6	1.020	1.023	1.020
	Night urine, 350 c.c.; nitrogen concentration, 1.1%	Night urine, 290 c.c.	Night urine, 260 c.c.

Time	No. 13 Aged 6 Yrs. Specific Gravity	No. 14 Aged 6½ Yrs. Specific Gravity	No. 15 Aged 6 Yrs. Specific Gravity
6- 8	1.025	1.024	1.015
8-10	1.032	1.027	1.025
10-12	1.035	1.024	1.015
12- 2	1.026	1.020	1.020
2- 4	1.027	1.021	1.025
4- 6	1.029	1.028	1.020
6- 6	1.029	1.028	1.010
	Night urine, 70 c.c.	Night urine, 200 c.c.	

DISCUSSION OF NORMALS

Normal children show about the same response to the nephritic test meal that normal adults do. It will be noted as one looks over the results obtained in the normal cases that there is considerable variation in the gravity of the two-hour specimens in each case. *In every normal case there is a difference of at least 8 points between the highest and lowest gravity of the two-hour specimens, and usually there is a difference considerably greater than this.* These tables show very well how in health the concentration of the urine is varied from hour to hour. In every normal case except one, the specific gravity of the night urine was over 1.020. The amount of night urine in the normals varied too much to be able to determine on any definite standard of normality. Sixteen nephritics were studied. These were various types of cases, some acute, some subacute or chronic, some mild, others severe. In most cases the phthalein test was made in addition to the test meal, for purposes of comparison, and in a few the determination of the concentration of blood urea nitrogen. No case was studied which was

edematous, as conditions of urinary excretion are changed in such a way by edema that the two-hour renal test does not apply to this group of cases.

ACUTE NEPHRITIS

Case 1.—R. M., aged 6 years. Severe acute nephritis. Urine: smoky; albumin, large trace; sediment shows many hyaline and granular casts, and many red blood cells. Time of test, one month after onset.

Time	Sp. Gr.	Time	Sp. Gr.
6- 8	1.018	2- 4	1.018
8-10	1.020	4- 6	1.018
10-12	1.020	6- 6	1.022
12- 2	1.018		

Blood urea nitrogen = 21 mg. per 100 c.c. blood.
Night urine 40 c.c.
Interpretation: Fixation of gravity at a moderately high level, characteristic of acute nephritis in the stage of repair; indicates that normal function has not yet returned.

Case 2.—H. K., aged 3⅔ years. Severe acute nephritis. Urine: albumin, trace; sediment shows many red blood cells and a rare cast. Phthalein excretion = 33 per cent. Time of test, three weeks after onset.

Time	Sp. Gr.	Time	Sp. Gr.
6- 8	1.010	2- 4	1.011
8-10	1.014	4- 6	1.013
10-12	1.013	6- 6	1.013
12- 2	1.015		

Night urine, 180 c.c.; nitrogen concentration, 1.06 per cent.
Interpretation: Fixation of gravity at a low level; phthalein test lower than it should be at this stage, indicating the possible development of a chronic process; night urine of low gravity, but with a normal nitrogen concentration.

Case 3.—J. C., aged 10 years. Severe acute nephritis. Urine: bright red; albumin, large trace; sediment shows many red blood cells, and a few bloody and granular casts. Blood urea nitrogen 32 mg. per 100 c.c. blood. Phthalein excretion = 40 per cent. Time of test, four days after onset.

Time	Sp. Gr.	Time	Sp. Gr.
6- 8	1.012	2- 4	1.014
8-10	1.015	4- 6	1.015
10-12	1.015	6- 6	1.015
12- 2	.....		

Night urine, 505 c.c.; nitrogen concentration, 0.67 per cent.
Interpretation: Marked fixation of gravity at a low level; low phthalein test; moderately increased blood urea, indicating retention of nitrogen; a decided nocturnal polyuria. All tests indicate a considerable degree of functional impairment.

Case 4.—J. M., aged 4 years. Severe acute nephritis. Urine: albumin, large trace; sediment shows many casts and red blood cells. Phthalein excretion = 75 per cent. Blood urea nitrogen = 19 mg. per 100 c.c. blood. Time of test, three weeks after onset.

Time	Sp. Gr.	Time	Sp. Gr.
6- 8	1.020	2- 4	1.020
8-10	1.020	4- 6	1.022
10-12	1.022	6- 6	1.022
12- 2	1.021		

Night urine 202 c.c.
Interpretation: Fixation of gravity at a high level; normal blood urea

and phthalein; clinically a severe case of nephritis, but with high functional tests. Here the two-hour renal test indicates a damaged kidney when the other tests give no indication of it.

CASE 5.—L. N., aged 5⁵⁄₁₂ years. Moderately severe acute nephritis. Urine: albumin, absent; sediment shows a few casts. Time of test, 1 month after onset.

Time	Sp. Gr.	Time	Sp. Gr.
6- 8	1.005	2- 4	1.020
8-10	1.017	4- 6	1.021
10-12	1.020	6- 6	1.025
12- 2	1.020		

Night urine, 200 c.c.; nitrogen concentration, 1.1 per cent.

Interpretation: No fixation of gravity; a normal response to the test meal; high gravity and nitrogen concentration of night urine. Tests indicate a kidney which has nearly recovered, and in which there is no chronic process developing.

CASE 6.—M. P., aged 5⅓ years. Mild acute nephritis. Urine: albumin, none. Sediment shows rare hyaline and granular casts. Phthalein excretion = 83 per cent. Time of tests, seven weeks after onset; boy clinically well.

Time	Sp. Gr.	Time	Sp. Gr.
6- 8	1.025	2- 4	1.024
8-10	1.023	4- 6	1.022
10-12	1.020	6- 6	1.030
12- 2	1.020		

Night urine, 170 c.c.; nitrogen concentration, 1 per cent.

Interpretation: No fixation of gravity; high gravity and nitrogen concentration of night urine; high phthalein excretion. Tests show, in conjunction with his good general condition, that he has practically recovered, and is in no danger of developing a chronic condition.

CASE 7.—R. I., aged 8 years. Moderately severe acute nephritis. Urine: albumin, trace. Sediment shows large numbers of red blood cells and rare cast. Phthalein excretion = 43 per cent. Time of tests, three weeks after onset.

Time	Sp. Gr.	Time	Sp. Gr.
6- 8	1.018	2- 4	1.015
8-10	1.018	4- 6	1.015
10-12	1.015	6- 6	1.018
12- 2	1.016		

Night urine, 230 c.c.; nitrogen concentration, 0.77 per cent.

Interpretation: Fixation of gravity at a low level; low concentration of night urine; low phthalein excretion. A damaged kidney, which still shows severe interference with function.

CASE 8.—S. B., aged 4 years. Acute nephritis. Urine: albumin, none. Sediment shows rare red blood cell. Boy clinically well. Phthalein excretion = 43 per cent. Time of tests, one month after onset.

Time	Sp. Gr.	Time	Sp. Gr.
6- 8	1.014	2- 4	.....
8-10	1.012	4- 6	1.015
10-12	1.015	6- 6	1.018
12- 2	1.015		

Night urine, 340 c.c.; nitrogen concentration, 0.70 per cent.

Interpretation: Fixation of gravity at a low level; large quantity of night urine with a low nitrogen concentration; low phthalein excretion. Although the boy is clinically well, and shows no albumin in the urine and little in the sediment, the functional tests indicate that his kidneys are not functioning

normally. This means that it is possible he is developing a chronic process, and would tend to make us watch him rather carefully for the next few months.

CASE 9.—J. M., aged 10 years. Acute nephritis. Urine: albumin absent. Sediment shows a rare granular cast and a rare red blood cell. Time of test, three weeks after onset.

Time	Sp. Gr.	Time	Sp. Gr.
6- 8	1.016	2- 4	1.011
8-10	1.010	4- 6	1.018
10-12	1.015	6- 6	1.020
12- 2	1.006		

Night urine 400 c.c.

Interpretation: No fixation of gravity; probably no impairment of function. This boy had a very marked response to the diuretic materials of the test meal, passing 1,260 c.c. of urine in the test twenty-four hours, with a fluid intake of only 900 c.c.

CASE 10.—J. W., aged 2⁵⁄₆ years. Mild subacute nephritis. Urine: albumin absent. Sediment shows a rare red blood cell and a rare cast. Time of test, three months after onset.

Time	Sp. Gr.	Time	Sp. Gr.
6- 8	1.016	2- 4	.....
8-10	1.005	4- 6	1.020
10-12	1.015	6- 6	1.024
12- 2	1.014		

Night urine 160 c.c.

Interpretation: No fixation of gravity. The good general condition of the child, and the normal response to the test meal show that he is developing no chronic process, although his urine has contained a few blood cells for a long time.

CHRONIC CASES

CASE 11.—M. H., aged 11 years. Very mild chronic nephritis. Urine: albumin, slightest possible trace occasionally. Sometimes the urine contains none. The sediment sometimes shows a rare cast. Blood urea nitrogen, 14 mg. per 100 c.c. blood. Phthalein excretion = 70 per cent.

Time	Specific Gravity	Salt Concentration, Per Cent.
8-10	1.010	0.60
10-12	.....	....
12- 2	1.010	0.62
2- 4	.....	....
4- 6	1.020	0.70
6- 8	1.020	0.94
8- 8	1.021	0.88

Night urine, 315 c.c.; nitrogen concentration, 0.92 per cent.

Interpretation: No fixation of gravity; no fixation of salt concentration; reasonably high gravity and nitrogen concentration of night urine; normal blood urea nitrogen and normal phthalein excretion. Functional tests together indicate that the nephritic condition is extremely mild, probably nonprogressive, and that as far as can be told from such tests, the function of the kidney is normal.

It is in just this type of case that functional tests are of the most value. Here is a girl who has had an acute nephritis, and whose urine has not cleared up as it should, still containing a little albumin and casts occasionally. If we can determine by our functional tests that the function of the kidney is normal, it aids us immensely in prognosis and makes us feel that the urine

will eventually clear up, and that the girl will not have a seriously progressive nephritis.

CASE 12.—F. L., aged 5½ years. Chronic nephritis of two years' duration; clinically severe. Urine: albumin, trace. Sediment shows many hyaline and granular casts. Phthalein excretion = 25 per cent.

March 23, 1916		May 7, 1917		May 8, 1917
Time	Sp. Gr.	Time	Sp. Gr.	Sp. Gr.
7- 9	1.007	6- 8	1.020	1.017
9-11	1.005	8-10	1.020	1.018
11- 1	1.008	10-12	1.019	1.019
1- 3	1.005	12- 2	1.018	1.018
3- 5	1.003	2- 4	1.020	1.018
5- 7	1.005	4- 6	1.018	1.019
7- 9	1.007	6- 6	1.019	1.019
9-11	1.007			

Interpretation: Marked fixation of gravity in 1916 at a low level; in 1917 at a fairly high level; very low phthalein excretion. The functional tests indicate a severely damaged kidney in which a permanent and probably progressive nephritis has developed.

CASE 13.—I. C., aged 10 years. Chronic nephritis of three years' duration. Although the child has had albumin and casts in the urine at every examination during the last two years, her general condition is excellent, and at a glance she would be taken for an unusually healthy child. Urine: albumin, slight trace. Sediment shows a few hyaline and granular casts.

Blood urea nitrogen = 9 mg. per 100 c.c. blood. Phthalein excretion = 50 per cent.

Time	Sp. Gr.	Time	Sp. Gr.
6- 8	1.021	2- 4	1.025
8-10	1.021	4- 6	1.025
10-12	1.022	6- 6	1.026
12- 2	1.026		

Night urine, 220 c.c.; nitrogen concentration, 1.4 per cent.

Interpretation: Moderate degree of fixation at a high level; night urine of high gravity and high nitrogen concentration; moderately low phthalein excretion; tests indicate moderate functional impairment. Taken in conjunction with the good clinical condition, they indicate a nephritis of mild character, probably not rapidly progressive.

CASE 14.—L. S., aged 7¼ years. Chronic nephritis of two years' duration; acute exacerbation; general condition poor; considerable anemia. Urine: albumin, slight trace. Sediment shows many red blood cells and granular casts. Phthalein excretion = 50 per cent.

Time	Sp. Gr.	Time	Sp. Gr.
6- 8	1.015	2- 4	1.015
8-10	1.015	4- 6	1.016
10-12	1.016	6- 6	1.017
12- 2	.....		

Night urine 350 c.c.

Interpretation: Marked fixation at a low level; large amount of night urine of a low gravity; moderately low phthalein excretion. In conjunction with the general poor condition the tests indicate a permanently damaged kidney, with an ultimately poor prognosis.

CASE 15.—H. P., aged 3 years. Chronic nephritis of one year's duration. Urine: albumin, trace. Sediment shows rare hyaline and granular cast. Blood urea nitrogen = 14 mg. per 100 c.c. blood. Phthalein excretion = 60 per cent.

Time	Sp. Gr.	Time	Sp. Gr.
6- 8	.....	2- 4	1.017
8-10	1.020	4- 6	1.018
10-12	1.020	6- 6	1.015
12- 2	1.020		

Night urine, 210 c.c.; nitrogen concentration, 0.70 per cent.

Interpretation: Fixation of gravity, during the day especially; low gravity and low nitrogen concentration of night urine; low normal phthalein excretion. We can say from the functional tests that the kidney at present is slightly damaged. Whether or not the damage will be permanent and progressive cannot at present be foretold.

Case 16.—J. G., aged 6 years. Chronic nephritis; acute exacerbation; tests made while he was eliminating edema. Urine: albumin, large trace. Sediment shows many hyaline and granular casts. Blood urea nitrogen = 25 mg. per 100 c.c. blood. Phthalein excretion = 50 per cent.

Time	Sp. Gr.	Time	Sp. Gr.
6- 8	1.011	2- 4	1.014
8-10	1.013	4- 6	.....
10-12	1.010	6- 6	1.020
12- 2	1.014		

Interpretation: Fixation of gravity during the day. The gravity is of little significance in this case as he was eliminating edema. The test diet caused a marked diuresis; his fluid intake was 900 c.c. and his output 1,365 c.c. for the twenty-four hours. With this diuresis he eliminated 10.9 gm. of salt on an intake of about half this.

Case 17.—F. O'L., aged 8 years. Chronic nephritis secondary to scarlet fever; two years' duration; acute exacerbation. Urine: albumin, large trace. Sediment shows numerous red blood cells and granular casts. Blood urea nitrogen = 16 mg. per 100 c.c. blood. Phthalein excretion = 59 per cent.

Time	Sp. Gr.	Time	Sp. Gr.
6- 8	.....	2- 4	1.019
8-10	1.017	4- 6	1.018
10-12	1.018	6- 6	1.016
12- 2	1.019		

Night urine 500 c.c.

Interpretation: Marked fixation of gravity with a large amount of night urine of low gravity. Phthalein excretion very slightly diminished. Blood urea normal. Two-hour renal test shows a diminution of kidney efficiency; other tests do not.

DISCUSSION OF "TWO-HOUR" RENAL TEST

The "two-hour" renal test is a test of kidney function that is particularly well suited for use in children, as it takes only a day to perform, complicated chemical analyses are not needed, and strict dieting is unnecessary. Fifteen normal cases were studied, and in none of them was there a fixation of gravity, or a night urine of low gravity; therefore, there is a good standard of normality. In nearly all the nephritis cases studied there was a definite fixation of gravity, sometimes to an extreme degree, and many cases showed a night urine of low gravity. The test is a very delicate one, probably more so than any other, and it is possible that relatively marked fixation of gravity may mean only slight functional damage. A good deal of caution is

necessary, therefore, in the interpretation of this test, and in stating an opinion on any given case it is best also to take into consideration the phthtalein test, the urinary examination, and the general clinical condition of the child.

Blood Urea Nitrogen.—It has long been recognized that end-products of protein metabolism are sometimes retained in the blood in cases of nephritis. The determination of the concentration in the blood of these products is considered to be a valuable diagnostic and prognostic aid. The concentration of urea nitrogen gives us a very good idea of the concentration of the nitrogenous end-products, and the urea nitrogen is the substance that is being used by most observers as an index of nitrogen retention.

Leopold and Bernhard,[9] studying normal children, found that there was a good deal of variation in the concentration of urea nitrogen in the blood. Their lowest figure was 8 mg. per 100 c.c. of blood, and their highest 21 mg., giving an average of 12 mg. for fifty cases. Inasmuch as only one of their normal cases was over 15 mg., and this one was a cardiac patient, who might well have had urea retention, it is fair to assume that any concentration of blood urea nitrogen over 15 mg. per 100 c.c. of blood is abnormal.

We have made blood urea nitrogen determinations on twelve nephritic children, using the urease method.

TABLE 4.—Blood Nitrogen Determination in Nephritic Children

Case	Urea Nitrogen Per 100 C.c. Blood, Mg.	Remarks
1. J. C.	32.0	Acute nephritis; no edema
2. W. K.	36.0	Acute nephritis; much edema; very scanty urine excretion
3. J. M.	11.6	Severe acute nephritis; considerable edema
4. H. K.	23.0	Severe acute nephritis; much edema
5. M. K.	46.0	Severe acute nephritis; much edema; died the next day
6. R. M.	21.0	Severe acute nephritis; much edema
7. F. O'L.	16.0	Chronic nephritis (mild)
8. M. H.	14.0	Chronic nephritis (mild)
9. H. P.	14.0	Moderately severe chronic nephritis
10. S. W.	24.0	Severe chronic nephritis; died three days later
11. J. C.	25.0	Chronic nephritis
12 J. C.	9.0	Chronic nephritis

DISCUSSION OF BLOOD UREA NITROGEN DETERMINATIONS

Of course, this series of cases is by far too small on which to base any conclusions. From a study of these few cases it would seem that in the severe cases of acute nephritis there may be considerable urea retention, and that a high blood urea warns us to be on the watch for uremia. The same information is given to us by the clinical condition

9. Leopold and Bernhard: Am. Jour. Dis. Child., 1916, **11**, 432.

of the patient. Most of the chronic cases of nephritis in children are so mild and so slowly progressive that there is no urea retention, or at least not enough to give us any information of value. From the little experience that we have had with blood urea determinations we should be inclined to conclude that they have comparatively little value in dealing with nephritis in children, and that they apply more particularly to the hypertensive cases with contracted kidneys, seen in adults.

SUMMARY AND CONCLUSIONS

Four methods of testing kidney function in children have been discussed: the added salt and urea test, the phthalein test, the two-hour renal test, and the determination of the concentration of urea nitrogen in the blood. Of these tests the added salt and urea test is of little practical value in children. The determination of the blood urea is probably of slightly more value. The most valuable of the four tests discussed are the phthalein test and the two-hour renal test, because they are simple to carry out, and because they give us reliable and important information concerning the functional power of the kidney. These two tests supplement each other, and more valuable information can be obtained by using them together than by using either one singly. I feel that these two tests are of unquestioned value, not in diagnosis, not as guides to treatment, but particularly in *prognosis*. The prognosis of nephritis in early life is most difficult, and who can say whether any given child with mild subacute or chronic nephritis will ultimately recover, or whether the nephritis will progress, with a finally fatal termination in a few years? We know that many of these patients recover entirely after one or more years of continuous or intermittent albuminuria, and again, that many of them develop a permanent chronic nephritis and die within a few years.

The tests for function, taken in conjunction with the general condition of the child, help us a good deal in giving an intelligent prognosis, but even with the tests we are often at a loss. In general, repeated *low* functional tests at intervals of a few months mean a poor prognosis. High phthalein excretion alone does not help us one way or the other. High phthalein excretion, normal blood urea, and a normal response to the two-hour test warrant a conclusion that the process is a mild one, that the kidneys are only slightly damaged, and that there is a good chance for ultimate recovery.[10] The diagnosis and treatment of nephritis in children is comparatively simple, but the prognosis is difficult and of great importance, and any simple laboratory tests that can help us in answering this question are worthy of general consideration and use.

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10. The question of prognosis will be taken up more in detail in a later paper.

THE PROPHYLACTIC USE OF PERTUSSIS VACCINE CONTROLLED BY THE COMPLEMENT FIXATION TEST *

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MINNEAPOLIS

During the past five years numerous clinical reports have been made on the prophylactic and curative value of pertussis vaccine. Graham,[1] Ladd[2] and Bamberger[3] reported favorably on its curative power in small doses. Hess[4] was fortunate in being able to observe the effect of vaccines during an epidemic of whooping cough in an institution; he was skeptical of its curative power, but was favorably impressed by its prophylactic value, even though 10 per cent. of his treated patients developed pertussis. Hartshorn and Moeller,[5] after reviewing the literature and reporting cases of their own, thought the vaccine worthy of further trial, but did not recommend its general use. Abt[6] says that "the possibility of immunizing by vaccination is still an open question for pertussis." Luttinger,[7] after an extensive experience with the whooping-cough clinic of the New York City Health Department, concludes that pertussis vaccine in large doses (that is, one-half billion, one billion and two billion bacteria) is of value in preventing whooping cough. In his most recent report[8] he says that "his results would warrant the routine administration of pertussis vaccine for both curative and prophylactic purposes." Von Sholly, Blum and Smith,[9] using the same material as Luttinger, conclude that "more observations and more critical observations with controls for comparison must be made before the case can be made out for the curative and prophylactic value of pertussis vaccine."

It was thought that this question could be attacked from a new angle. The observations on the results of vaccines made thus far have been chiefly clinical. If vaccines are of value it would be natural to

* Submitted for publication June 11, 1917.

* From the Department of Pediatrics and the Department of Pathology and Bacteriology, University of Minnesota.

1. Graham, E. E.: Am. Jour. Dis. Child., 1912, **3,** 41.
2. Ladd: Arch. Pediat., 1912, **29,** 581.
3. Bamberger: Am. Jour. Dis. Child., 1913, **5,** 33.
4. Hess, A. F.: Jour. Am. Med. Assn., 1914, **63,** 1007.
5. Hartshorn and Moeller: Arch. Pediat., 1914, **31,** 586.
6. Abt: Arch. Pediat., 1916, **33,** 881.
7. Luttinger: New York Med. Jour., 1915, **101,** 1043.
8. Luttinger: Jour. Am. Med. Assn., 1917, **68,** 1461.
9. Von Sholly, Blum and Smith: Jour. Am. Med. Assn., 1917, **68,** 1451.

expect that after their administration specific antibodies would be present in the blood. We have two methods for determining the presence of specific antibodies — the agglutination and complement fixation tests. The agglutination test in pertussis has been tried by many workers, Shiga,[10] Wollstein,[11] Povitzsky and Worth[12] and others, and all agree that it is far from satisfactory. The complement fixation reaction, however, has been more successful. Bordet and Gengou,[13] using the bacillus discovered by them as antigen, found a positive complement fixation test in all cases of pertussis. Bächer and Menschikoff[14] found positive complement fixation in pertussis only after the injection of vaccine, but clinically noticed no benefit from the use of the vaccine. Shiga, Imai and Eguchi[10] were able to differentiate between *B. influenza* and the Bordet-Gengou bacillus by means of complement fixation. Wollstein[11] in nine cases of pertussis was unable to make the complement fixation test react positively. Olmstead and Povitzsky[15] found that "the separation by morphologic and cultural characteristics of the typical Bordet-Gengou bacillus from atypical strains of the Bordet-Gengou bacillus and from the influenza bacillus has been confirmed by complement fixation tests." Winholt[16] found a positive complement fixation obtainable two weeks, but stronger about eight to ten weeks, after the onset of the disease, and that when the influenza bacillus was used as antigen with serum of pertussis patients, no complement fixation occurs. Friedlander,[17] by a slight modification of technic, obtained positive complement fixation in all cases of pertussis even in the early catarrhal stages.

It was, therefore, proposed to select a number of healthy children who, as far as could be determined, had never had whooping cough, and vaccinate them with different pertussis vaccines, in order to study the effect of such treatment on antibody formation, by means of the complement fixation test.

TECHNIC

Two types of vaccines were employed:[18] a commercial vaccine, purchased in the open market, and a vaccine made by the ordinary method of heating the bacteria for one hour at 60 C. The latter was standardized, in the usual manner, by counting against the red blood corpuscles of normal blood. Two

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10. Shiga, Imai and Eguchi: Centralbl. f. Bakt., abt. 1, 1912.
11. Wollstein: Jour. Exper. Med., 1909, **11,** 41.
12. Povitzsky and Worth: Arch. Int. Med., 1916, **17,** 279.
13. Bordet and Gengou: Ann. d. l'Inst. Pasteur, 1906, **20,** 218.
14. Bächer and Menschikoff: Centralbl. f. Bakt., abt. 1, 1912, **61,** 218.
15. Olmstead and Povitzsky: Jour. Med. Research, 1916, **33,** 379.
16. Winholt: Jour. Infect. Dis., 1915, **16,** 397.
17. Friedlander and Wagner: Am. Jour. Dis. Child., 1915, **8,** 135.
18. I am indebted to Dr. W. P. Larson for valuable assistance with the laboratory work.

different strains of Bordet-Gengou bacillus were used, one obtained from the New York City Department of Health and the other from a commercial biological house.

The technic of the complement fixation tests was that ordinarily used. About 1 c.c. of the patient's blood was drawn and allowed to coagulate; the serum was separated in the centrifuge and heated to 56 C. for ten minutes (we find that ten minutes is sufficient to inactivate the serum and there is less danger of impairing its antibody content); in the tests 1 to 2 drops of undiluted serum from a capillary pipet (of which about 20 drops make 1 c.c.) was taken. The amboceptor consisted of antisheep rabbit serum (1:40). The antigen was prepared by scraping, in distilled water, a forty-eight hour growth of *Bacillus pertussis* on blood agar and shaking for twelve hours, after which it was incubated at 48 C. for twenty-four hours. The antigen was standardized against the blood serum of a known case of pertussis.

The attempt was made to immunize rabbits by injecting prophylactic doses of vaccines and, at the same time, inoculating control rabbits with living Bordet-Gengou bacilli. A comparison of the antibody production of living and dead bacilli was rendered impossible by the fact that many rabbits gave a positive complement fixation test before treatment was begun. The tests had, therefore, to be made entirely on humans. For this purpose fairly normal and healthy children, ranging from 6 months to 3 years, were chosen from the inmates of Lymanhurst, City Children's Hospital.

In all, seventeen patients were treated; these were divided into three series. In the first series of four cases, three were given vaccine prepared by us and one a commercial vaccine, once a week for four weeks; the first two doses were one hundred million bacilli, and the last two doses two hundred million. Blood for the complement fixation test was taken before each injection, and again two weeks after the last injection. All tests were absolutely negative. In the second series of four cases, all were given our vaccine, two hundred million being given once a week for five weeks. Complement fixation tests performed before each injection and one performed two weeks after the last injection were, likewise, all negative. In the third and last series, the dosage recommended by the New York City Health Department was used; one half billion, one billion and two billion bacteria were given at two-day intervals. There were nine cases; of these, five received our vaccine and four received commercial vaccine. Of the five who received freshly prepared vaccine, three reacted positively and two were negative. Of the four cases receiving commercial vaccine, one reacted positively and three negatively. In this last series of nine cases the ages ranged from 6 months to 3 years. The ages of those giving positive reaction were 12, 24, 26 and 36 months, respectively; of those giving negative reactions, 6, 14, 14½, 16 and 20 months.

SUMMARY AND CONCLUSIONS

Our observations in seventeen cases would theoretically justify the prophylactic vaccination against pertussis.

In none of the cases treated with the smaller doses could any antibodies be demonstrated. Whereas, large doses, such as recommended by the New York City Health Department, showed antibodies in 44 per cent. of the cases. The freshly prepared vaccines were, apparently, more effective than the stock vaccines, as 60 per cent. of the patients treated gave positive fixation reaction. From this, it may be concluded that it is possible to immunize children against pertussis if sufficiently large doses of freshly prepared vaccine be used.

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PAROXYSMAL TACHYCARDIA IN CHILDHOOD *

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The function of originating and transmitting the automatic impulses which result in the contraction of the heart belongs to certain specialized tissues which represent the remnant of the primitive cardiac tube. These excitation waves have been shown to arise at the junction of the superior vena cava with the right auricle, in the upper portion of the sino-auricular node. From here they pass through the node and are transmitted by numerous paths to the auricular musculature and to the atrioventricular node described by Tawara. From this node stimuli pass through the bundle of His and into its branches, which divide and subdivide until their ramifications form an intricate network by means of which the impulses are rapidly distributed to the ventricular myocardium. As impulses travel downward through these conducting fibers, the heart responds by sequential contractions of the auricles and ventricles. Under certain conditions, however, any portion of this conducting system may acquire the function of originating the excitation wave, producing variations in rate and rhythm and occasionally a complete reversal of the cardiac mechanism.

Vagal influences or a local lesion may so depress the normal point of origin that some other locality may assume the rôle of pacemaker. A lesion of the auricular or ventricular myocardium or endocardium may increase the sensitivity of some portion of this specialized tissue and likewise establish an abnormal rhythm. Lesions may directly involve any of the conducting fibers, most frequently those at the atrioventricular node, and produce a delay in transmission or an actual blocking of the excitation wave, which in some instances reaches its destination by an abnormal and more circuitous route. The conductivity of these tissues may also be so reduced by the transmission of impulses arriving with excessive frequency that a functional delay or even a fatigue block may result. All of these conditions affect the electrocardiographic picture and the characteristic changes are now well recognized.

In auricular flutter and in paroxysmal tachycardia the heart contracts in response to excitation waves of ectopic origin which arise below the sino-auricular node at a rate of 200, or more, a minute. In both conditions the auricle responds to each stimulus, but the ven-

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* From the Pediatric and Medical Clinics of the Johns Hopkins Hospital.

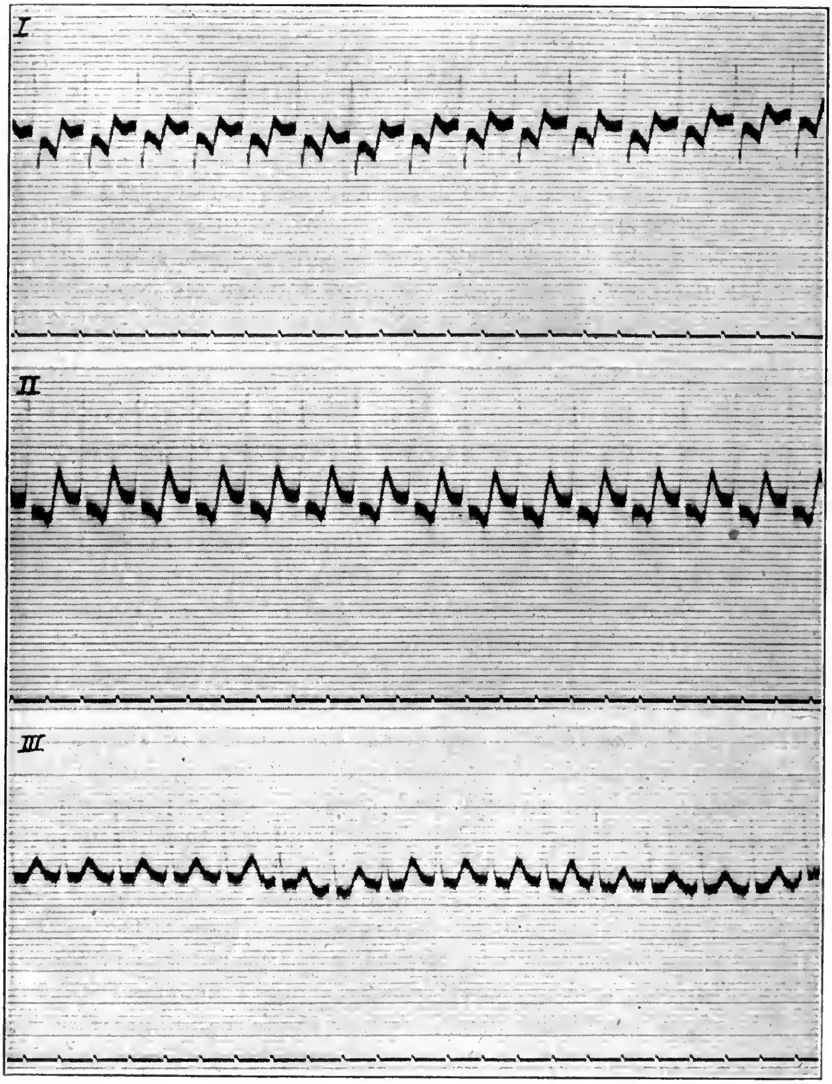

Fig. 1.—Electrocardiogram taken during paroxysm. Derivations I, II and III. Rate, 196.5 per minute. The P wave is represented by a deflection between S and T. Standardized; 1 cm. deflection = 1 millivolt. Time recorded in fifths of a second.

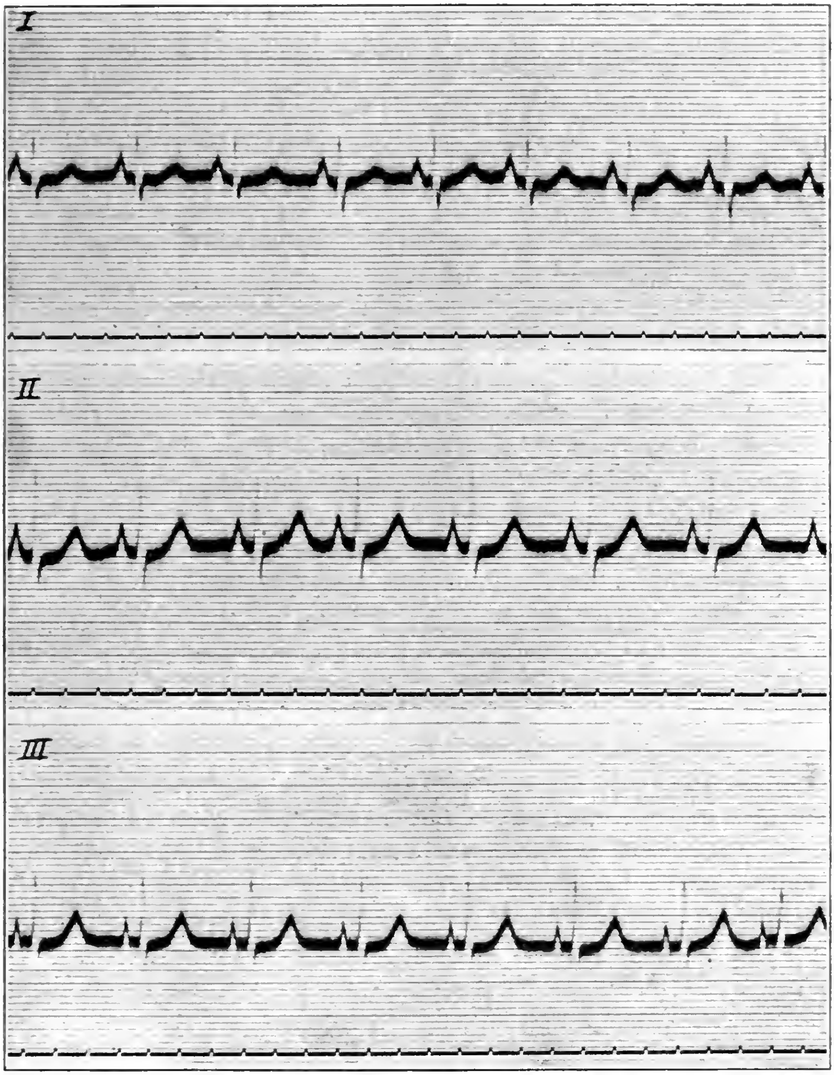

Fig. 2.—Electrocardiogram taken between paroxysms. Derivations I, II and III. Rate varies from 96 to 103 per minute. Standardized; 1 cm. deflection = 1 millivolt. Time recorded in fifths of a second.

tricular response is largely dependent on the ability of the conducting fibers to transmit excitation waves at this rapid rate. In paroxysmal tachycardia the auricle seldom acquires a rate of more than 200 in adults or of 250 in children. In flutter the rate is usually between 240 and 360 per minute. When this rapidity of auricular contraction is reached it is commonly associated with a functional or fatigue block at the atrioventricular node or in the bundle of His, permitting only a certain proportion of the impulses to pass. This has led to the application of the term "auricular flutter" to those conditions of auricular tachysystole in which the auricular rate is in excess of the ventricular, the former often being exactly two or more times the latter. An auricular flutter, once established, tends to persist, although the degree of functional block may vary from time to time. A suitable distinction for clinical purposes may be based on the transient character of paroxysmal tachycardia and the absence of a ventricular deficit.

While transient tachycardia of ectopic origin is not among the common disorders of the adult heart, yet it is encountered with sufficient frequency to excite but passing comment. That this condition rarely occurs during childhood is evident from the scarcity of reported cases, notwithstanding the attention which, during recent years, has been given to disturbances of the cardiac rhythm. Wilson,[1] in discussing the tachycardias of children, includes paroxysmal tachycardia with auricular flutter under the term "auricular tachysystole." Several cases of the paroxysmal type are mentioned in his contribution. Of 29 cases of paroxysmal tachycardia reported by Lewis, only one was in a child. In a series of 33 cases reported by Hart[2] one was in a girl, who, at the age of 9, had her first attack. The published reports of 9 cases in which a tachycardia of the paroxysmal type, as distinguished from auricular flutter, occurring in children under 10 years of age, have been collected, and the prominent features are here tabulated.[3] The youngest patient in which this condition has been observed is that reported by Lewis.[4] The child was only 3 months of age. In two of the reported cases, paroxysms began during the third year, in two during the sixth, and in one during the seventh year of life.

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1. Wilson, F. N.: Recent Progress in Pediatrics, Am. Jour. Dis. Child., 1915, **10,** 376.

2. Hart, T. S.: Abnormal Myocardial Function, 1917, p. 95.

3. In addition to the cases in the table, there are in the records of the Mt. Sinai Hospital electrocardiograms of several children which show typical paroxysmal tachycardia. These were included in the electrocardiographic exhibit of that institution at the Annual Meeting of the American Medical Association, New York, 1917, but are still unpublished.

4. Lewis, T.: Lectures on the Heart, 1915, p. 117. (Delivered at McGill University, 1914.)

The occurrence of paroxysmal tachycardia in young children has been brought to our attention by the case of a patient recently admitted to the Harriet Lane Hospital in the service of Dr. John Howland, who has kindly furnished the clinical data for the following report.

REPORT OF CASE

M. P. L., a sturdy boy 3½ years of age, was admitted May 12, 1917, to the Harriet Lane Home of the Johns Hopkins Hospital, suffering from frequent attacks of tachycardia. He is the younger of two children, his brother being in perfect health. His parents are living and well. At birth the patient weighed 7¼ pounds. When 3 months of age he weighed 12 pounds. At this time artificial feeding was begun and various milk modifications were employed. Nutritional disturbances were constant during the year and a half following. At 12 months the child weighed only 11½ pounds. During this period he had frequent attacks of vomiting and it was noticed that at these times the heart's action was extremely rapid. The vomiting was so persistent that a diagnosis of probable pyloric stenosis had been made.

During his second year he was placed on a more liberal diet, and his condition began to improve. Since then he has developed normally and remained in excellent health. During the past year he has vomited three times, but only once on each occasion. The attacks of rapid heart action have continued, coming usually every three or four days, sometimes more often. Occasionally several weeks have elapsed between attacks. The parents become aware of the presence of the tachycardia by a pallor of the child's face, slight engorgement of the veins of his forehead and by the excessive and rapid pulsation in his neck. He becomes somewhat fretful and less active, but usually continues his play and suffers no apparent inconvenience. The attacks last from two to thirty-six hours, usually three or four; begin abruptly without premonition and stop suddenly. It has been thought that excitement and excessive activity might be contributing factors. On the contrary, the tachycardia has occasionally developed while the child was asleep.

He was examined May 12 by Dr. Howland, who reports:

"He is a well nourished, alert, active child. The posterior cervical glands on the left side are moderately enlarged. There is no other glandular enlargement. The tongue is clean. The apex is in the fourth interspace, in the nipple line. There is a slight sinus arrhythmia. There is a cardiorespiratory murmur heard best in the second right interspace, close to the sternum, heard only during midexpiration. It is heard also in the interscapular region behind. The lungs are normal; spleen not palpable; von Pirquet reaction negative."

May 14 the child experienced a typical attack. During the morning while playing out of doors a slight pallor of his face was noticed and a rapid, forcible pulsation of the jugular vein was observed. He was entirely free from discomfort, and continued bright and playful. The pulse was about 200. After two hours the attack subsided and the pulse dropped to 112. The patient was discharged May 15. Reports indicate that the paroxysms have since then been of less frequent occurrence. There were no attacks during the first three weeks in June.

Electrocardiographic records were obtained May 13, 14 and 15. One of these was taken during the paroxysm which occurred on the 14th. The rate computed from the electrocardiogram is 196.5 per minute. The sequence is normal. Following an R wave of supraventricular origin, there is, in the first and second derivations, a deep S, interrupted in its ascent by an inverted P wave, which, with the ascending limb of the following T, results in a large diphasic curve. In the third derivation the P wave is represented by a small oscillation between the R and T waves. Conductivity is diminished, the P-R interval measuring 0.21 second. The electrocardiogram is typical of a paroxysmal tachycardia of auricular origin (Fig. 1).

REPORTED CASES OF PAROXYSMAL—

Reported by	Date	Age	Sex	Predisposing Factors	Age When Paroxysms Began, Yrs.	Number of Paroxysms	Duration of Paroxysms	Normal Pulse
Buckland,[5] F. O.	1892	11	♀	Measles; neurotic temperament	5	Numerous; two attacks observed	12 hours to 10 days	84 to 96
Herringham,[6] W. E.	1898	11	♀	Scarlet fever during infancy; tonsillitis; constipation	5	Seven in 10 months	18 hours to 13 days	80 to 96
Merklen,[7] P.	1901	13	♀	....	Not stated	Occasional	12 hours to 8 days	80
Hay,[8] John	1907	6	♂	"Delicate constitution"	6	Frequent; almost continuous for six months	Few seconds to 10 days	84
Hume,[9] Wm. E.	1913	6	♀	Occurred during convalescence from diphtheria after antitoxin treatment	6	Numerous on 41st and 51st days of illness	"Short and long periods"	88
Kidd,[10] Percy	1914	4½	♂	Measles..............	2	About once each month; frequent during last six months	Fewminutes; later almost continuous	80
Hutchinson,[11] R., and Parkinson, J.	1914	2¾	♂	No previous illness; well nourished	2¼	Four in five months	12 hours to 12 days	64 to 80
Lewis,[4] Thomas	1914	3 mos.	..	....	3 mos.	....	Several hours	....
Hart,[2] T. S.	1917	10	♀	....	9	....	....	....
Personal observation	1917	3½	♂	Gastrointestinal disorders and malnutrition during infancy	During 1st yr.	Usually every 3 or 4 days	2 to 36 hours	90 to 112

Electrocardiograms taken on the 13th and 15th have a normal rhythm and a normal sequence. That taken on the 15th shows a rate which varies from 96 to 103 per minute. There is a moderate sinus arrhythmia. The P wave in the first derivation is slightly notched. The S deflection is deep in the first and second derivations. Conductivity is normal, the P-R interval measuring 0.14 second. The electrocardiogram is normal (Fig. 2).

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5. Buckland, F. O.: Case of Rapid Heart, Tr. Clin. Soc. Lond., 1892, **25,** 92.
6. Herringham, W. P.: A Case of Paroxysmal Tachycardia, Tr. Clin. Soc. Lond., 1898, **30,** 99.
7. Merklen, T.: Tachycardie paroxystique essentielle chez l'enfante, Semaine méd., 1901, **31,** 164.
8. Hay, John: Paroxysmal Tachycardia (Case 2), Edin. Med. Jour., 1907, **21,** 40.
9. Hume, W. E.: Irregularities in Diphtheria (Case 4), Heart, London, 1913, **5,** 25.
10. Kidd, Percy: Paroxysmal Tachycardia in a Boy Aged Four and a Half Years, Brit. Jour. Child. Dis., 1914, **11,** 264.
11. Hutchinson, R., and Parkinson, J.: Paroxysmal Tachycardia in a Child Aged Two and Three-Fourths Years, Brit. Jour. Child. Dis., 1914, **11,** 241.

—TACHYCARDIA IN CHILDREN

Pulse During Paroxysm	Paroxysm Begins	Paroxysm Ends	Accompanied by	Subsequent Course	Graphic Records
200 to 215	Abruptly, with arrhythmia	During sleep	Pallor; dizziness; rapid breathing; low fever	Probable recovery	None
200 to 256*	Abruptly; often with sudden movement	Always during sleep	Languor; slight cyanosis; cardiac dilatation; enlargement of liver; jugular pulsation	Recovery	None
220	Abruptly	Abruptly; often with coughing and hemoptysis	Dyspnea; cardiac dilatation; epigastric hyperesthesia; hemoptysis	Unknown	None
182 to 230	Abruptly; sometimes with vomiting	Abruptly; often with periods of arrhythmia	Pallor; listlessness; pulmonary edema; cardiac dilatation; hepatic enlargement; jugular pulsation	Recovery	Polygram; ventricular venous pulse during paroxysms; numerous auricular extrasystoles as attacks subside
225	....	....	Collapse; nausea and vomiting; cardiac dilatation	Recovery	Polygram; tachycardia apparently of nodal origin; extrasystoles precede paroxysm
240	Abruptly; with momentary collapse	Abruptly; sometimes after vomiting	Cardiac dilatation; hepatic enlargement; general anasarca; dyspnea	Fatal termination; probably from malignant endocarditis	None
160 to 245	Abruptly; sometimes with momentary collapse	Abruptly; once after defecation; often with arrhythmia	Vomiting; cardiac dilatation; slight edema; enlarged and pulsating liver; partial suppression of urine; jugular pulsation	Recovery	Polygram; ventricular venous pulse during paroxysms; electrocardiogram; R modified by inverted P; nodal origin (?)
270 to 290	....	....	....	....	Electrocardiogram; inverted P between R and T; probably auricular tachycardia
....	....	....	....	....	Electrocardiogram
180 to 200	Abruptly; no premonition	Abruptly; with sense of relief; often during sleep	Slight pallor; lessened activity; jugular pulsation	Reduction in frequency and severity of paroxysms	Electrocardiogram; inverted P with beginning of T wave; auricular tachycardia

From a theoretical standpoint the excitation waves of paroxysmal tachycardia may originate in the lower portion of the sino-auricular node, in the wall of the auricle, in the atrioventricular node, in the bundle of His and its branches, or in the ventricle. Electrocardiographically, three types are recognized: auricular, nodal (atrioventricular) and ventricular. In this instance the form of the ventricular complex, Q-R-S-T, eliminates a tachycardia originating below the node of Tawara. Were the impulses originating in the atrioventricular node, the P wave would be more likely to fall with, or nearer to, the wave of ventricular excitation. In this case the P deflection is removed from the preceding R by a distance equivalent in time to 0.11 second. The presence of an inverted P indicates an impulse of ectopic origin arising in the auricle probably near the atrioventricular node. The prolonged conduction time, as measured from the inverted P to the following R, results from bundle fatigue due to the very frequent stimuli which this

structure is called on to transmit. The consistent form of the atypical P waves suggests that the stimuli come from a single focus. It is reasonable to conceive of this tachycardia as a rapid succession of extrasystoles, originating at some point in the auricle which, during the paroxysm, assumes the rôle of pacemaker.

The etiology of paroxysmal tachycardia is obscure. Alcohol, tobacco, gastro-intestinal disturbances, inflammation of the upper respiratory tract, infectious diseases, arthritis, endocarditis, nephritis, hypertension and coronary sclerosis have been mentioned as predisposing causes. In the series collected of paroxysmal tachycardia in children under 10, diphtheria, measles and scarlet fever are given as predisposing factors. One is described as having a "delicate constitution," while another is "well nourished, with no previous illness." The case here described has suffered from none of the infectious diseases of childhood, and the only possible predisposing condition was the early malnutrition resulting from digestive disturbances. Since the paroxysms continue and the child is in perfect health, it is necessary to assume the existence of some local lesion or defect. Whether this is a temporary depression of the sinus, such as has been produced experimentally in animals, with an escape of the auricle, or whether there is a point of hypersensitivity in the auricle with a high rate of stimulus production, it is not possible to determine. Vomiting is frequently associated with these tachycardias. This may point to slight digestive derangements, perhaps unrecognized, but sufficient to incite the paroxysm. On the other hand, the persistence of attacks over considerable periods of time during which the patients are in perfect health discounts such a supposition.

The paroxysms are usually accompanied by more or less circulatory embarrassment, and in prolonged attacks by cardiac dilatation and other signs of myocardial exhaustion. The prognosis is dependent on the ability of the heart to maintain its function during protracted paroxysms. Of the ten tabulated cases, five are reported as having recovered, while only one led to a fatal termination, and this was probably due to a malignant endocarditis which complicated the tachycardia. In young children without other cardiac disorders the prognosis is evidently favorable, and with the observation of reasonable precautions the paroxysms tend to become shorter, to occur less frequently and ultimately to disappear.

No consistent results have been obtained from medication. Various remedies have been employed only to be discarded. In the series tabulated it is interesting to note that vomiting, coughing and defecation sometimes accompany the cessation of the paroxysm, suggesting the influence of reflex inhibitory stimulation. Pressure on the vagus, ocular pressure and holding the breath have occasionally, in adults,

been followed by a termination of the attack, but usually none of these procedures is successful. Digitalis is useful when evidences of myocardial insufficiency are present, but its administration has no apparent effect on the tachycardia. All possible sources of local irritation or infection should be removed. Rest and quiet during the paroxysm, a suitable diet, proper elimination, and a life free from unusual excitement, constitute the the treatment of uncomplicated cases.

CLINICAL DEPARTMENT

A CASE OF PNEUMONIA OF UNUSUALLY SHORT DURATION *

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Abortive pneumonia is the term applied by Wunderlich[1] to that class of cases presenting the clinical picture of pneumonia together with the usual signs of pulmonary consolidation, yet running an exceedingly brief and mild course, often terminating by crisis on the second or third day. Credit is given Eugen Seitz by Krafft[2] for first describing this condition. Following him it has been described under various names, pneumonic febricula (Bernheim), peripneumonic synocha (Marrotte), hemopneumonia (Woillez), and rudimentary pneumonia (Finkler). The later reports of Bechtold[3] in 1905, and of Krafft[2] and Kerr[4] in 1910, have made the condition more or less familiar.

The statement of Aufrecht[5] that the so-called abortive pneumonia is far more frequent than the reported cases would indicate, is probably correct. Because of the brevity of the disease, many cases are not seen by the physician and the diagnosis in any event is a difficult one except with the aid of accessory diagnostic measures.

The clinical picture has been analyzed in the reports mentioned. Except in duration, it does not differ materially from that of pneumonia running the usual course. The onset is usually sudden, with prostration, high fever, rapid respiration, pain in the side and cough. Typical "rusty" sputum is frequent with older patients. Kühn[6] says that herpes is more common in this than in the usual type of disease.

The presence and nature of the physical signs are variable. In the majority of cases reported there is a high pitched or dull percussion note, with crackling râles and suppressed breathing over a limited area. These signs may be present from the onset, but more frequently come out from twelve to fourteen hours later. The changes usually persist for from one to five days after the temperature becomes normal.

* Submitted for publication Aug. 5, 1917.
* From the Harriet Lane Home of the Johns Hopkins Hospital.
1. Wunderlich: Specielle Pathologie und Therapie, Stuttgart, 1856, **3,** 2.
2. Krafft: Dissertation, Jena, 1910.
3. Bechtold, A.: München. med. Wchnschr., 1905, **52,** 2113.
4. Kerr: Med. Rec., New York, 1910, **77,** 701.
5. Aufrecht, E.: Spec. Path. u. Therap., Nothnagel, 1899, **14,** 128.
6. Kühn, See G.: Diseases of the Lungs, 1891, **2,** 180.

In two of Bechtold's cases, one of Krafft's, and one of Kerr's, there were no physical signs to be elicited.

The bacteriologic evidence of abortive pneumonia is exceedingly meager. In one of Krafft's cases the pneumococcus was found in the blood; in two it was in the sputum. The organism has never been grouped.

As to the pathology of these cases, there are no available data, since there is no mortality. There has been much speculation as to whether the process passes through the stages of congestion and hepatization as in the usual pneumonia or is arrested sooner. The opinion is generally held that the process does not pass beyond the stage of congestion. Many authors, however, like Bechtold,[3] have preferred to leave the question open, or like Norris,[7] have been content to state that in such cases the consolidation is usually not complete.

The Roentgen ray affords some help in solving this problem. It is assumed by many roentgenologists that it is only when the inflammatory process in the lungs has progressed to the stage of cellular exudation that a shadow is cast.[8] In this regard the following case is of interest.

REPORT OF CASES

Case 1.—D. B., aged 4 years. Onset March 20, with pain in the left side, slight cough, rapid respiration and fever. He continued feverish and drowsy with rapid respiration. Examination on the fourth day showed a fairly well nourished boy, somewhat drowsy, breathing rapidly and with an occasional slight cough. There was marked herpes on the upper lip and about the left nostril. Temperature, 103 F.; respirations, 44; pulse, 120; leukocytes, 33,000. There were no changes detected on auscultation and percussion. On the following day there were distinct dulness on percussion and crepitant râles over the lower left back. On the sixth day the roentgenogram showed nothing suggestive of pneumonic consolidation. The signs and symptoms of pneumonia and the leukocytosis persisted. On the ninth day the roentgenogram showed the shadow of pneumonic consolidation of the left lower lobe. The disease terminated by crisis on the eleventh day and recovery was uneventful.

This case of frank lobar pneumonia gave clear physical signs of consolidation on the fifth day and yet there was no shadow cast until the ninth day. Shall it be assumed from this that an intense congestion may give the signs of consolidation and that a cellular exudate may not occur until the seventh or eighth day of the disease? Or shall it be assumed that a cellular exudate was present earlier but was not sufficiently dense to cast a shadow? At what point of the inflammatory reaction and by what physical condition the Roentgen-ray shadow is cast is still an open question. It is difficult to use this evidence, therefore, in the interpretation of the pathology of abortive pneumonia.

7. Norris, G. W.: Modern Med., Osler and McCrae, Ed. 2, Phila., 1913, **2,** 237.
8. Baetjer, F. H.: Personal communication, 1917.

Certainly the following case strongly suggests that the process may in some cases at least go on to the stage of hepatization.

CASE 2.—C. D., aged 3 years, was admitted to Harriet Lane Home, Dec. 16, 1916.

Past History.—Measles at 15 months; pneumonia on the right side lasting ten days and complicated by empyema. Following operation he made an uneventful recovery. November 1, six weeks before the present admission, the child was taken suddenly ill with headache, vomiting, pain in the right side and cough. He was admitted to the hospital with a temperature of 103.2 F.; leukocytes 34,500 and frank signs of consolidation of the right middle lobe. The blood culture was negative. The disease ran the usual course of pneumonia and terminated by crisis on the seventh day. Recovery was uneventful. The roentgenogram taken just before his discharge showed a slight diffuse shadow in the right side of the thorax low down, which had probably been present since the empyema, sixteen months previous.

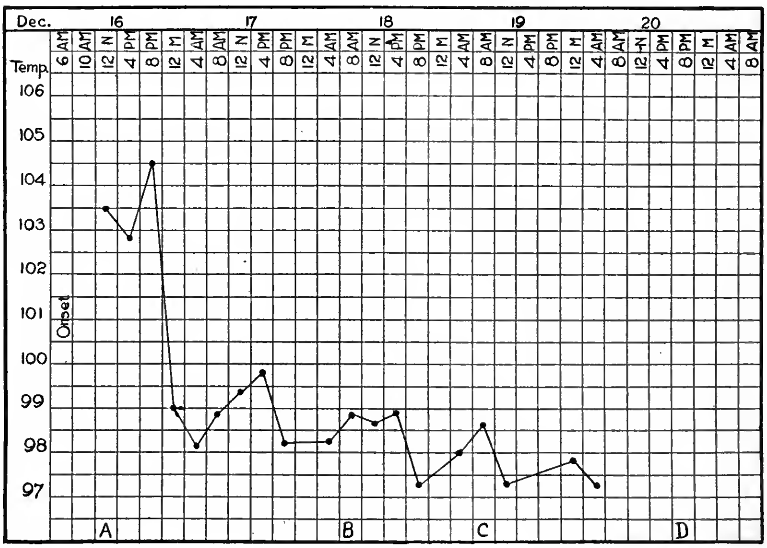

Fig. 1.—Temperature chart of a case of pneumonia, showing crisis eighteen hours after onset. *A,* white blood cells, 38,900; *B,* first roentgenogram; *C,* white blood cells, 11,000; *D,* second roentgenogram.

Present Illness.—The child was taken suddenly at 6 a. m., December 16, with headache, vomiting, high fever and rapid respiration.

When examined at 10 a. m. his cheeks were flushed. The temperature was 103.6 F., the pulse 144, the respirations 44 and the leukocytes 38,900. The chest was well formed and moved normally. There was the scar of the empyema operation below the angle of the right scapula. The dull percussion note and distant breath sounds heard over the right lower back were attributed to the thickened pleura. There was no other change detected on auscultation and percussion. The diagnosis of pneumonia was made on the history of sudden onset, the prostration and rapid breathing and the leukocytosis.

The examination at 8 p. m. showed the condition unchanged; temperature 104.5 F.; pulse, 144; respirations, 44. Defervescence occurred by crisis and at

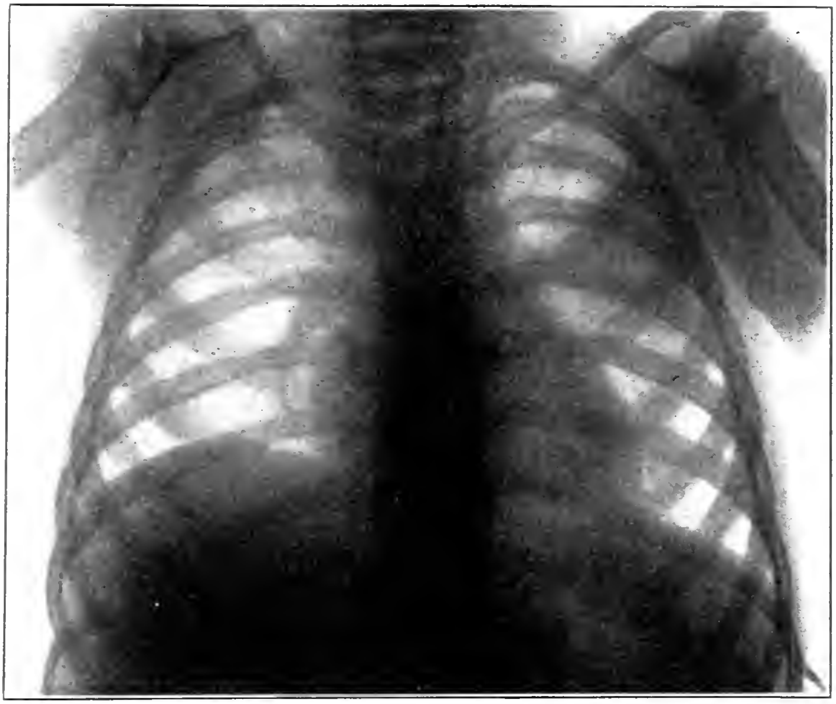

Fig. 2.—Roentgenogram showing triangular area of consolidation in the upper part of the left lung.

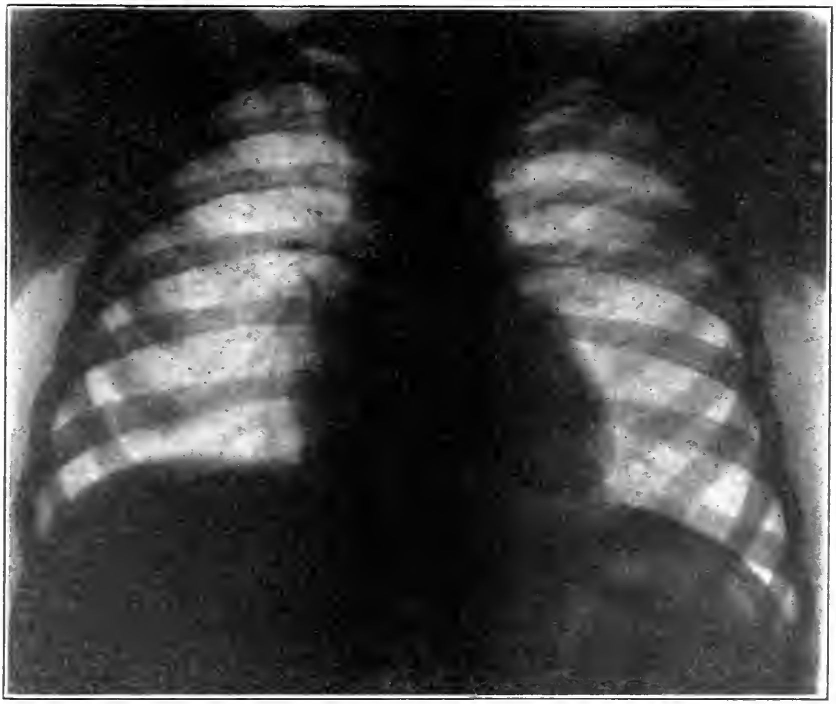

Fig. 3.—Roentgenogram showing resolving consolidation at the upper part of left lung.

12 midnight; eighteen hours after the onset his respiration was quiet and easy, his temperature 99 F., and his pulse 100.

The temperature did not rise above 100 F. subsequently. The following day the patient was sitting up, bright and apparently free from discomfort. The roentgenogram (Fig. 2) showed a triangular area of consolidation peripherally located in the upper part of the left lung.

December 19, leukocytosis, 11,000. Recovery was complete.

Roentgenogram December 21 (Fig. 3), four days after the crisis, showed very slight remains of the consolidation.

The history of the above case is typical of pneumonia save in its duration and the absence of physical signs. The absence of the latter may be understood when the location of the lesion is considered. As shown by Mason,[9] consolidation peripherally located may give no changes that can be detected by auscultation. An impaired percussion note over the affected area was probably present, but was obscured by the absence of a normal note on the other side for comparison.

I have not been able to find in the literature another case of the so-called abortive pneumonia of which roentgenograms were made.[10]

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9. Mason, H. H.: Am. Jour. Dis. Child., 1916, **11,** 188.

10. Other case reports: Weil, A.: Ein Fall von eintägiger Pneumonie, Berl. klin Wchnschr., 1879, **16,** 665. Simon: Zur Kasuistik der abortiven Pneumonie, München. med. Wchnschr., 1908, **55,** 1837. Engels: Zur Kasuistik ephemer. Pneumonien, München. med. Wchnschr., 1908, **55,** 2088. Pollatschek: Zur Kasuistik der abortiven Pneumonie, München. med. Wchnschr., 1908, **55,** 2089. Ruhl: Zur Kasuistik der abortiven Pneumonie, München. med. Wchnschr., 1908, **55,** 2391.

CASE OF PERNICIOUS ANEMIA IN A BOY OF EIGHT YEARS *

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History.—Martin A. was born in August, 1908, in a small settlement in the woods of northeastern Maine and had always lived there. His parents were healthy. Four other children were alive and well; two had died in infancy of indigestion. There had been no miscarriages.

Martin was born at full term, after a normal labor. He was nursed for eighteen months and then given a general diet. He had measles when he was a year old and whooping cough when he was 4 years old. Otherwise he had always been well.

When he was 5 years old, he began to complain of being tired. He did not look well and became very pale, the skin taking on a yellowish tinge. He did not feel well enough to go to school, but was not confined to bed. He improved somewhat after six months, but soon relapsed. Since then his general condition had, on the whole, deteriorated. He was treated for a short time in the Eastern Maine General Hospital, at Bangor, when 6½ years old. The examination of his blood made there at that time was as follows:

Hemoglobin (Dare)	28 per cent.
Red blood corpuscles	1,600,000
White blood corpuscles	8,000

Both fresh and stained smears of the blood showed great variation in the size, shape and color of the red cells. About one-half of the cells were in the form of rings. They were somewhat stippled, but very few nucleated red cells were seen. A differential count showed:

	Per Cent.
Small lymphocytes	35.0
Large lymphocytes	4.0
Large mononuclears	3.66
Transitionals	1.0
Polymorphonuclear neutrophils	51.6
Polymorphonuclear basophils	0.66
Normoblasts	2.33
Unclassified	1.66

The stool at that time was formed and light-brown in color. It showed no fermentation and no microscopic blood, but contained several large food particles. No ova or parasites were seen. The Wassermann test made there was negative.

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*From the Medical and Pathological Services of the Children's Hospital.

When he was 7 years old, he was sick in bed for five weeks with a high fever and difficulty in breathing. His parents did not know what was the trouble. During the last six months he had been able to be up and about the house, but had had a poor appetite. His bowels had moved normally and the stools were thought to have been normal. He was admitted to the Children's Hospital Nov. 9, 1916, when 8 years and 3 months old.

Physical Examination.—He was fairly developed and poorly nourished. He was very pale, and there was a slight yellow tinge to the pallor. The superficial veins of the scalp were dilated and there was some edema of the back of the head. The nose and ears were normal. The tongue was pale and clean. His teeth were much decayed and there was an abscess about the left inferior six-year molar. The gums were fairly healthy. The tonsils were of moderate size and apparently healthy. The lungs showed nothing abnormal. The area of cardiac dulness extended 3 cm. to the right and 9 cm. to the left of the median line. There was a sharp systolic murmur at the aortic area, with a slight diastolic murmur down the middle of the sternum. There was a soft systolic murmur at the apex and a sharp, high-pitched diastolic murmur at the apex. The second pulmonic sound was louder than the second aortic sound. There was both a capillary and a Corrigan pulse. There was a pistolshot and marked double murmur in the groin. The systolic blood pressure was 118 and the diastolic between 45 and 50. There was a marked systolic blowing sound in the vessels of the neck. D'Espine's sign was absent. The abdomen was soft and tympanitic; there were no evidences of fluid or of new growths. The lower border of the liver was felt 5 cm. below the costal border in the nipple line. The spleen was not palpable. The genitals were normal. The extremities were normal. There was no spasm or paralysis. The knee jerks were equal and normal. Kernig's and Babinski's signs were absent. There were a number of lymph nodes in the neck, the size of marbles and almonds, those on the left being somewhat larger than those on the right. There was no enlargement of the other peripheral lymph nodes. The skin was dry and scaly. It was fairly dark-brown over the abdomen and in the axillae. There were one or two brownish patches on the legs. The scrotum was also somewhat pigmented. The mouth, however, showed no discolorations. The examinaton of the fundi showed nothing abnormal, except extreme pallor.

The examination of the blood at entrance was as follows:

Hemoglobin (Sahli)	15 per cent.
Red blood corpuscles	860,000
White blood corpuscles	8,000
Small mononuclears	61.0 per cent.
Large mononuclears	11.0 per cent.
Polynuclear neutrophils	25.0 per cent.
Eosinophils	0.5 per cent.
Basophils	2.5 per cent.

The red corpuscles showed little achromia, but marked variations in size and shape. There was a tendency to a predominance of large forms. There was an occasional stippled red cell. The platelets numbered 12,900. Ten normoblasts and one megaloblast were seen to each 200 white cells.

The urine was clear, acid, of a specific gravity of 1.011 and contained the slightest possible trace of albumin, but no sugar, acetone or bile. The sediment showed a few epithelial cells. It contained no casts or urobilinogin.

The stool was soft, acid in reaction, golden-brown in color, sour in odor. It contained no neutral fat or fatty acids, but a little soap. It showed a considerable amount of starch. No parasites or ova were seen. There was apparently a slight increase of urobilinogin in the stool.

The Wassermann and tuberculin tests were negative. Blood cultures were negative.

During the patient's stay in the hospital his temperature was usually between

100 F. and 101 F., sometimes a little lower, sometimes a little higher. His decayed teeth were extracted and the jaws and gums made healthy, without any improvement in his condition. He had no diarrhea. Repeated examinations of the stools showed constantly a slight amount of soap, but starch was never found again. An examination for occult blood, when he had been on a hemoglobin-free diet for a number of days, showed none. Parasites and ova were sought for carefully many times, but were never found. The urine never contained albumin again. The blood showed no improvement. The examination of the blood November 28, the day before his death, was as follows:

Hemoglobin (Sahli)	10 per cent.
Red corpuscles	570,000
White corpuscles	6,200

Differential count:

Small mononuclears	47 per cent.
Polymorphonuclear neutrophils	53 per cent.

The red cells showed marked variation in size and shape. Six normoblasts, one stippled cell, three polychromatophilic cells and two or three degenerated cells were seen in counting 200 white cells.

Treatment.—He received no specific treatment except one intravenous injection of 20 c.c. of whole blood with 4 c.c. of 10 per cent. solution of sodium citrate. It had been intended to try repeated injections of small amounts of blood, but his death prevented this method of treatment from being carried out.

His general condition steadily deteriorated from the time of his entrance to his death, November 29.

The diagnosis of pernicious anemia seemed very positive in this instance, although no cause for it could be made out. It hardly seemed possible that the decayed teeth and alveolar abscess could be the cause of his trouble, for while secondary anemia with leukocytosis is not uncommon as the result of decayed teeth and diseased jaws and gums, the toxemia from them would hardly be sufficient to cause so severe a condition as pernicious anemia. Addison's disease was suggested to a certain extent by the discoloration of the skin. The absence of profound muscular weakness, the normal systolic pressure and the slightly elevated temperature showed, however, that there was no adrenal insufficiency. The pigmentation could, moreover, be easily explained as the result of blood destruction. It was felt that the enlargement of the heart, the murmurs in the heart and neck, the high pulse pressure and other evidences of aortic insufficiency were not due to organic disease but to muscular weakness and vasomotor insufficiency.

The necropsy was performed December 2, by Dr. S. Burt Wohlbach and Dr. S. B. Marlow. Dr. Wohlbach's report is as follows:

Necropsy.—At the Children's Hospital, Dec. 2, 1916, on Martin A., aged 8 years.

Anatomic Diagnoses.—Anemia; emaciation; fatty degeneration of heart, liver and kidney; hypertrophy and dilatation of heart; edema of lungs, pericardium and scalp; hyperplasia of bone marrow, accompanied by marked thickening of calvarium. *Ascaris lumbricoides.*

Microscopic Diagnoses.—Acute bronchitis; acute parenchymatous degeneration of kidneys.

Body: The body is that of a well developed, emaciated white boy. The skin of the whole body is uniformly olive-brown in color. There is deeper brownish pigmentation in the axillae and gluteal folds. The abdomen is protuberant and tympanitic. There is complete absence of hair in the axillae and pubic regions. The hair of the head is sparse and fine in texture. The mucosa of the mouth, pharynx and conjunctivae is very pale. The sclerae are porcelain white, and the vessels contain no blood. Rigor mortis is complete and there is slight postmortem settling of blood.

Peritoneal Cavity: Subcutaneous fat is reduced to a very small amount. It is a light canary-yellow in color. Abdominal muscles are pale and on section are wet. Lower border of liver lies 6 to 8 cm. below costal margin. Anterior abdominal wall and intestines adjacent to the gallbladder are stained a deep yellow. Pelvis contains a few cubic centimeters of clear, yellowish liquid. Appendix is small, normal in appearance. There is a Treve's fold present. The bladder is distended with urine and reaches to the level of the umbilicus.

Thoracic Cavity: No free liquid, no adhesions; no exudate.

Pericardial Cavity: The pericardium is markedly distended with slightly turbid straw-colored liquid, 120 c.c. in amount.

Heart: The heart is large; right side is dilated; weighs 240 gm. The epicardium is pale and at the base of the heart it encloses clear, yellowish liquid. It is elevated by this liquid to a thickness of 1 to 3 mm., so that the vessels of the surface of the heart appear to be depressed. There is a small amount of bright yellow fat in the epicardium. The myocardium is soft and pale. It is mottled throughout with grayish-yellow areas. The endocardium everywhere presents an almost uniform wavy linear, yellowish marking, running transversely to the direction of the muscle fibers, giving an unusually marked and typical tigroid mottling. The apexes of the papillary muscles are light grayish-yellow in color. The valves and endocardium are normal in appearance. Measurements: tricuspid 9 cm., pulmonary 5.5 cm., mitral 7 cm., aortic 4 cm. The wall of the right ventricle is 7 mm. in thickness; left 12 mm.

Lungs: On removal they partially collapse. Both are pale in color, the anterior halves being pinkish-gray, the posterior halves light salmon-red in color. The lobules are distinctly outlined. The alveoli are prominent and inflated. On the anterior border of both lungs there are areas where the alveoli are markedly distended. On section the cut surfaces yield much thin salmon-red liquid and a small amount of air. The cut surfaces are uniform throughout. The bronchial mucosa is bright pink in color and contains glassy yellow, viscous material.

Gastro-Intestinal Tract: The stomach is normal. Duodenum, jejunum, ileum and colon are normal. Nine *Ascaris lumbricoides* are found in the small intestine. Most of them are immature and range in length from 5 to 10 cm. Other parasites were carefully searched for but were not found.

Liver: This is normal in size; weighs 980 gm.; color is light red with a minute, yellowish mottling. On section the cut surfaces are pale yellowish-red with minute deeper yellowish points and areas which involve the central portion of the lobules. The bile ducts and gallbladder on section are normal.

Pancreas: This organ is normal in size and consistency. On section the cut surfaces have a distinctly yellowish cast. The blood vessels are somewhat prominent as pink dots.

Spleen: This weighs 85 gm.; the capsule is smooth, not wrinkled; the consistency is normal. On section, the cut surfaces are maroon-red in color; the trabeculae are just visible; malpighian bodies appear with normal prominence.

Kidneys: Combined weight 280 gm.; they are large; both are identical in appearance. The perirenal fat has the same yellow color as the rest of the fat in the body. The kidneys are pale in color, normal in shape; the capsule strips readily from its smooth surface. On section the cut surfaces of the cortex appear as pale yellowish and of more than normal opacity. The average width is 6 mm.

The glomeruli are visible as minute colorless dots. The pyramids are pale; otherwise normal. The ureters are normal in size; not dilated.

Adrenals: Both are normal in appearance, except for the presence in the cortex of small nodules 2 to 3 mm. in diameter. Some of these project from the surface of the cortex.

Pelvic Organs: Bladder and genitalia are normal.

Organs of Neck: Tongue, tonsils, pharynx, larynx, trachea and esophagus are normal; thyroid glands are normal; the two parathyroids were dissected out and found to be normal in appearance.

Aorta: Normal throughout. The size is normal for a child of this age.

Head: The subcutaneous tissues of the scalp are markedly thick, due to distention with yellow liquid, which runs freely from the incision. The calvarium, after reflection of the scalp, presents a remarkable appearance. It is dark reddish-purple in color and the surface of the bone is irregular owing to the presence of mound-like elevations or bosses. There are prominent elevations situated symmetrically on the frontal bones and on the parietal bones. These measure roughly 3 cm. in diameter and are elevated approximately 0.5 cm. above the surface of the surrounding calvarium. The bone saws with unusual ease and the surfaces yield much deep-red, pasty marrow. The whole skull is markedly thickened and through the bosses the thickness averages 1 cm. The internal and external tables are very thin, less than 0.5 mm. in thickness, while the thickness of the bone is composed of loose cancelous bone enclosing a large amount of soft, deep-red marrow. The dura and sinuses are normal.

Brain: This is normal in appearance, normal in consistency. Nothing abnormal found on section of the hemispheres, basal ganglia, pons, medulla and cerebellum.

Middle Ears: Normal.

Pituitary: The pituitary body appears normal.

Mesenteric Lymph Nodes: The mesenteric lymph nodes are large, yellowish, with reddish centers. The bronchial lymph nodes are similarly enlarged. The retroperitoneal lymph nodes are enlarged and similar in appearance to the mesenteric. The peripheral lymph nodes are enlarged.

Microscopic Examination.—Heart: The fibers of the inner part of the myocardium show many minute vacuoles; otherwise the myocardium is negative.

Lung: Moderately injected; occasional alveoli contain a few strands of fibrin and numerous polymorphonuclear and large mononuclear cells containing brown granular pigment in about equal numbers. The bronchioles contain masses of polymorphonuclear leukocytes with few mononuclear phagocytic cells.

Spleen: Deeply injected. The malpighian corpuscles are of fair size. The reticular tissue of the pulp seems reduced in amount and contains a relatively small number of lymphocytes. In the sinuses are occasional small groups of cells resembling myelocytes; large mononuclear cells with basophilic cytoplasm. There are also numerous mononuclear and polynuclear eosinophils in the reticular tissue. Occasional nucleated red blood corpuscles are found in the sinuses.

Liver: The centers of the lobules show moderate injection with blood. The liver cells about the central vein covering areas of about a fourth of the radius of the lobule are filled with small vacuoles, giving the cells a spongy appearance. The sinusoids for the most part contain but little blood and no adventitious cells except an occasional mononuclear eosinophil. There is a small amount of light brown pigment in granular form in the liver columns and in the endothelium of the sinusoids.

Kidney: Moderately injected. The glomeruli are negative. The convoluted tubules, distal and proximal, and ascending Henle tubules, show marked dilatation and are filled with circular reticulum and granular material. The epithelium of these tubules is ragged, granular, irregular in amount and faintly stained. Many nuclei are vesicular, small and densely stained. In places the tubules are almost denuded of epithelium, only a narrow fringe of granular cytoplasm remaining.

All types of tubules contain considerable brown granular pigment in the epithelium cells.

Pancreas: Adrenals, thyroid, jejunum, ileum and colon are negative. In the jejunum there is extensive postmortem desquamation of epithelium from the villi.

Bone Marrow of Femur: There is no fat present. The marrow is wholly myeloid tissue with comparatively few normal and nucleated red blood corpuscles. Among the nucleated red corpuscles are many abnormally large ones, of irregular shapes and lobed nuclei (megaloblasts). There are many mononuclear eosinophils (myelocytes) in groups, throughout the sections. The predominately myelocyte occurs in groups and is characterized by a large vesicular nucleus and a small amount of finely granular, basic staining cytoplasm. Mitoses are fairly numerous. Megakaryocytes are sparsely distributed and of small size.

Calvarium: The spaces between the bone trabeculae are filled with active myeloid tissue similar to that found in the femur.

Epicrisis.—The anatomic and microscopic findings in this case admit no other diagnosis than pernicious anemia. The marked thickening of the calvarium, due to a compensatory hyperplasia of the marrow of the diploe, is worthy of note.

The findings of the necropsy justify the clinical diagnosis of pernicious anemia. They show no possible cause for the disease, except the round worms which were found in the intestine. It does not seem reasonable, however, to believe that these worms were the cause of the severe anemia. In the first place, round worms are common in childhood; pernicious anemia is very rare. Moreover, when anemia is apparently due to round worms, it is of a secondary type, and mild. In this instance, while there were a number of worms in the intestines, they were all young. Furthermore, no ova were found in the feces on repeated examinations. It seems reasonable to believe, therefore, that the round worms had been recently acquired and that they had no etiologic connection with the patient's anemia.

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PROGRESS IN PEDIATRICS

RECENT PROGRESS IN OTOLOGIC DISEASES OF CHILDREN *

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During the past twenty-five years progress in the surgical treatment of suppurative otitis media achieved by the classical Schwartz and his followers in Europe, together with many American otologists, has brought this special branch of surgery to the foremost ranks. It has been the means of saving innumerable lives of children. It has saved them from being hopelessly deaf. It has made them selfsustaining and fitted them well for their life work; whereas, prior to this time many of them had been made public charges. While this branch of otology has progressed with great rapidity, not so much can be said for the treatment for the nonsuppurative forms of deafness.

During the past year a great deal of conscientious work has been done along the lines of teaching the deaf child to be a selfsustaining and a useful citizen. Dr. Max A Goldstein[1] of St. Louis, offers a classification of psychological principles in their application in the education of the deaf child, namely: 1. Observation. 2. Concentration. 3. Imitation. 4. Memory. 5. Correlation. 6. Imagination. 7. Rhythm and Mechanics.

1. Observation. First he shows that the faculty of observation in the deaf child is developed largely through the sense of touch or through the sense of sight, and the fact remains that tactile impressions are our most reliable and tangible forces for stimulating the child's mind.

Assuming that the child 5 years of age is totally deaf and has had no special or technical training at this time of his development, he has acquired many of the habits, manners and acts of normal children, but his power of observation has been seriously handicapped by the limited avenues through which his mental functions are stimulated.

Gestures, gymnastics, special movements of the tongue, lips and palate are used for the training of sight. Recognition of form is accomplished by a combination of the sense of sight and touch.

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1. Goldstein, Max A.: The Psychological Study of the Deaf Child, Laryngoscope, 1916, **26**, 1129.

The use of blocks and geometrical solids to stimulate the touch and sight faculties is an effective method of sense training and may be considered in various stages:

(*a*). The child is shown a geometrical solid and is then asked to select same by sight from a number of different shaped solids.

(*b*). The child is directed to feel a solid object while closing the eyes and is then asked to recognize the same object by sight. This correlates his sense of sight and sense of touch.

(*c*). The child is shown a solid object and then selects same by sense of touch with eyes closed. This is the reverse of the second step.

(*d*). From a series of blocks of different shapes the child is asked to select one block by sense of sight. This block is then returned to the rest of the collection and the child directed to select it by sense of touch alone. This sharpens the tactile sense for comparative sizes of lines and surfaces.

(*e*). Two blocks of slight variation in size and shape are presented to the child; he selects one by sense of touch and is then required to find that particular block from a larger group of objects.

In similar manner the pupil learns to differentiate textures and irregularities of surfaces, and the touch sense is so acutely sensitized by constant practice that he is eventually enabled to distinguish the difference in vibrations of musical tones, the differential vibrations of the voice in the throat and chest, which is a vitally important factor in technical training. Not only does this practice develop his powers of observation, but it also stimulates his faculties of concentration, memory and correlation.

2. Concentration. One of the real difficulties encountered in the early training of the deaf child is his lack of concentration. In reading, independent study, and other mental activities, the advanced deaf pupil has the advantage of being able to concentrate his mind on his work without the added extraneous diversions of noise and all forms of sound to which the normal hearing child is subjected. On the other hand, the deaf child not only sees, but also hears through the sense of sight and is constantly on the alert for all visible changes in the schoolroom, and in his surroundings even when attempting to concentrate his attention on the individual work prescribed for him.

When a photographer desires to pose a prattling, restless, lively baby before a camera, he arrests his attention by holding some bright or unusual object before the child at a fixed point. This momentarily arrests the child's attention and gives the photographer his opportunity for a picture. A crying baby is cajoled by a rattle or other sound, a moving, bright object, clapping of the hands, sudden change of position, patting on the body, or any of the other numerous resources

employed to arrest the child's attention. Attention is the basis of concentration; concentration is an indispensable aid to teacher and child.

Our deaf child, therefore, must have his attention engaged in some familiar way by which faculties already alert may be stimulated.

In the classroom a favorite method of developing the power of attention in the young deaf child is the use of matching exercises. Matching colors and objects not only trains the eye, but develops memory and concentration. Even though the child may not know the names of the colors he is asked to compare, he instinctively cultivates a comparative color sense by such practice. By the use of matching charts the teacher studies the dawning of the child's attention faculty and the child becomes more interested in the work of the teacher and in the acquisition, day by day, of new ideas. He cultivates concentration and the pleasure of learning. The more attractive we can make the form and character of the child's daily instruction, the more readily will we get his cooperation.

3. Imitation. One of the fundamental principles in the education of the child is imitation. Imitation is the foundation on which we build gesture, expression, speech and all voluntary movement. It, therefore, is utilized as one of the most valuable aids in child training.

Imitation develops almost simultaneously with observation. The first use of the organs of speech, as the tongue and lips, and the use of the breath, are taught through observation and imitation. The child that has never spoken a word is shown a feather or a slip of paper. The teacher holds the feather or the paper close to the mouth and blows lightly and sharply on it. The child sees the act and feels the impulse of breath and is directed to imitate it. The result is the letter p, t, f or some breath consonant, depending on the position of the lips and tongue. The differentiation of these breath consonants soon becomes apparent and the way is prepared for more complicated sounds.

The positions and movements of the tongue are both observed and imitated. Quick hand movements and gestures give the child additional opportunities for imitation. From the combination of movements of the tongue and lips, speech is gradually evolved. Correct breathing is acquired with somewhat more difficulty. Incidentally, it might be added that insufficient attention has been given to breathing and breath control in the training of the deaf child and in the correction of defects of speech.

Imitation is further accentuated by directing the child to reproduce objects that it sees and movements that are made. Three marbles are held up from a box of marbles; the child is directed to produce the

same number of marbles, and this his faculty of imitation soon enables him to do. Two kindergarten sticks are placed at right angles to each other; the child is asked to reproduce this position, and when this has been effected, he is asked to draw lines on the board in the same position. If he does so correctly from the objects before him, observation and imitation have been called into question. If he draws the object on the blackboard without seeing it, another faculty is being stimulated.

4. Memory. Memory combines the three previous faculties, observation, concentration and imitation. Memory is required to produce speech, to perform an act, to spell a word, to call a name, and to reproduce any process of mental activity.

The normal child first acquires speech by meaningless repetition of some elementary sounds. Before the babe can say "mama" it prattles "mamamama" or sounds like "papapapa" without significance. This principle has been recognized as the basis for teaching speech to the deaf.

Miss Josephine Avondino, of the Central Institute for the Deaf, whose work along this line has been especially intensive, in describing her "system of babbling," says:

> The movements of the muscles of the body of a very young infant are but evidences of the instinctive impulse to act, and, specially, the movements of the lips and tongue and the cooing of a baby are the instinctive preparation for speech. This elementary stage of vocalization soon passes and he reaches the babbling stage. This stage extends over a long period until definite sounds and syllables are gradually acquired.

The cultivation of memory for the acquisition of speech in the deaf child is of even greater importance than memory training for the normal child.

5. Correlation. The essential principles of observation, concentration and imitation are the a, b, c to the acquisition of speech. To this we add memory for the reproduction of speech, but there is still a vital factor necessary to the unfolding and higher development of the child's mentality — the comprehension of speech. A child may be taught the word mother. It may then be told that the word mother applies to a definite person. These two mental impressions may exist independently in the child's mind. The climax of these impressions, however, does not become apparent to the child until he realizes the relationship between the word mother and the person to whom the word applies. This association of ideas, or, as we have classified it, correlation, constitutes one of the most subtle refinements in the psychologic study of the deaf child.

When correlation becomes active in the scholastic work of the deaf child, his mind receives a tremendous stimulus, and from that time we note a decided advancement, not only in his scholastic, but also in his

speech work, facility of expression, and working ambition. A practical example of this unfolding of the child mind is presented in the following case:

E. M., a girl of 7, was admitted to the Central Institute for the Deaf, September, 1914. She was born deaf; functional tests corroborated this statement. There were not even tone islands of hearing; at a distance of 6 inches the child was able to repeat the vowels ah, oh, when called into the ear in a loud voice; the differentiation was uncertain.

This little girl is now in her second scholastic year of oral training; she reads, writes and speaks with fair fluency as compared to a normal child in the same period of training. Her speech is fluent, her voice flexible and well modulated. As soon as this child was able to comprehend, read, and speak phrases and sentences, it occurred to me to apply the principles of reeducation as advanced by Urbantschitsch, Bezold, Gradenigo and others. I was astonished to find after a few trials that this child could perceive spoken words and phrases when called into the ear with a moderate volume of voice. Today she is getting her training not only by speech reading and articulation, but by actual auricular exercises. She can even repeat sentences containing words of which she does not know the meaning and her oral training progresses much more rapidly with the assistance of her increasing hearing capacity.

We have been taught that in the congenitally deaf child the organ of Corti shows but an atrophied remnant of filaments of the cochlear nerve. What, then, has been the reconstructive or regenerative status that has taken place in this child's auditory perceptive mechanism? Reeducation of the deaf implies, as its name would indicate, the restimulation of a sensory apparatus that at some time was active. In this case, however, there had never been an active auditory sense, and the actual hearing capacity of today must be regarded as a new and constructive feature and not as a reeducation or reconstruction. What the psychologic element stimulated in this case might be, I am as yet not prepared to say.

I would say that the marked stimulation in this child's mentality and speech began at the time when the association of ideas or correlation of words and thoughts was first developed.

6. Imagination. Independence and facility of expression are best developed by cultivating the power of imagination. Recently the editor of one or our influential daily newspapers visited the Central Institute and related an interesting story to a number of our pupils of 11 or 12 years of age. The story contained, perhaps, about a thousand words. The raconteur is a man with a full beard and his speech is rather nervous and rapid. Six of our children listened to the story and acquired the subject matter entirely by lip reading. They were given a pad and pencil and asked to write the story as they had received it. The written story by each of the six children was expressed with individuality, conciseness, and accuracy. The essentials were maintained, but in each instance the form and character of the story was

reconstructed in accordance with the mentality and imaginative ability of the pupil. It was interesting to note how much variation could be given by these child minds in this instance. Imagination, as a psychologic element in child training, offers splendid opportunities for independence of expression, and it is in this form of practice that such facility of expression is developed.

M. W., an 8-year-old girl, lost her hearing completely at 3 years of age following an attack of cerebrospinal meningitis. She has been a pupil of the Central Institute for two years. Recently she was given a picture chart and asked to write the story which the picture suggested to her mind.

The imaginative sense expressed by this child is the more remarkable when we consider that her home surroundings are somber and her nature serious. With the stimulation of her imaginative faculty, additional sunshine is injected into her scholastic work and a new impetus given to the child's ambition. Cultivating the imaginative sense materially assists the child in language construction and develops actual, rather than abstract, expression. Imagination stimulates originality and actively assists in enriching the child's vocabulary.

7. Rhythm. An unconscious accessory in child training is the mechanical or automatic correlation of movement in the perception of vocal expression of thought or action. A number of our pupils have been taught to vocalize the musical scale comprising a whole octave. These pupils hear no sound. The notes that they produce with a fair degree of accuracy are evoked by purely mechanical means. They are taught tone placing, the position of the larynx, direction and projection of the voice, the control of breath and the intensity of voice vibration. Their tones are even sustained and mechanically correct. Their control is measured entirely by the tactile sense, especially the sensation of vibration and the differentiation of resonance. Tyndall has made the pertinent observation that light, sound, heat and electricity are all phenomena produced by waves of motion, varying only in degree, quality and intensity.

An ingenious adjunct in the training of the deaf has been introduced by a progressive eastern teacher. By the use of the piano the deaf child is trained to interpret differences in pitch of a vibrating note or chord. We have used this training constantly with our pupils. The pupil stands with his eyes closed and his fingers resting lightly on some part of the wooden piano case, or in some instances the pupils stand with their back to the key-board some distance from the instrument, depending on the transmission of vibrations through the floor. They can differentiate the bass chord from the middle register; a middle register from the upper clef, and these notes or chords can be struck in every variation and interpreted by the pupils with accuracy.

The physical principle involved in this experiment is obvious; the lower the pitch of the note the fewer the number of vibrations per second; the higher the pitch of the note, the more frequent the vibra-

tions per second. It is not the hearing faculty of the pupil, however, which makes this tone differentiation possible, but the actual sharpened tactile sense by which the difference in rapidity of vibration of a sustained tone is perceived.

The value of this mechanical production of the musical scale or the interpretation of the musical vibration to differentiate the pitch of a note has an important and significant application in our work with the deaf. There is a characteristic and almost invariably present monotone in the speech produced by the deaf and it is to overcome this noticeable defect in speech production that we lay unusual stress on the mechanics of voice production. By increased flexibility of voice, greater accuracy in pitch, better volume and more natural placement, we hope to reach such a high degree of efficiency that this characteristic monotone may be eliminated.

Dr. Lester Mead Hubby[2] reports on the "Experimental Treatment of Three Congenitally Deaf Children with Sonorous Vibrations," using an instrument called the Zund-Burguet electrophone, which covers the range of the human voice, and consists of about the same harmonics. By means of the three registers the timbres of three voices, low, medium and high, are produced. The employment of the vibration can be instantly varied to stimulate each ear according to its separate requirements. The intensity of the sound can be ranged sufficiently so that the length of the treatment is not fatiguing to the patient or the operator. The tones can be maintained at a given intensity as long as necessary. In its essential details, the instrument consists of three faradic hammers whose lengths can be altered by means of levers, with telephonic ear receivers.

The author states that in treating these three patients he used in the first case forty-seven treatments, twice on school days and once on Saturdays and Sundays. Each treatment lasted about three minutes. The second patient received fifty-five treatments, at the same intervals, and the third, forty-nine treatments.

He sums up his results as not encouraging so far as sufficient improvement of hearing to be of any practical benefit to the child, yet it would seem that the treatment would be of value in inculcating the concept of tone, and so of inflection, in those just beginning to learn to speak.

Mr. John Dutton Wright,[3] director of the Wright Oral School for the Deaf, New York City, who has done a great deal of work in reeducation of residual hearing, commenting on the Zund-Burguet apparatus, states that the aim of all efforts to increase sound percep-

2. Hubby, Lester Mead: Larngoscope, 1916, **26,** 1152.
3. Editorial: Laryngoscope, 1916, **26,** 1052.

tion is, primarily, to give the patient a greater and easier comprehension of spoken language; that is, to increase the usefulness of the residual hearing. He believes that the problem involves two distinct parts: first, the effort to increase the actual power of perceiving sounds within the range of the speaking voice; and second, the education of the brain more successfully to interpret the meaning of the imperfect sounds perceived.

Mr. Wright, who cooperated with Dr. Hubby in the treatment of the three patients heretofore mentioned, says that all three children were classed in most schools as totally deaf, because there was not a sufficient power of sound perception to differentiate between vowel sounds, no matter how loudly shouted at the closest range, until they had received a long series of exercises for the education of the brain to recognize and discriminate between sounds.

The three patients mentioned had, for some months prior to the series of treatments given by Dr. Hubby, received this educational auricular training, previous to which none of them had been able to recognize any word by ear.

In conclusion, Mr. Wright says that such tests would seem to establish the fact that there are many cases of children too deaf to acquire speech without special instruction and who cannot be benefited by mechanical auricular training, who can, however, be educated to interpret the imperfect sounds that reach them and thus acquire a certain ability to comprehend speech through the ear.

In gaining access to the mind through the ear by means of spoken language we are following the path trodden for millions of years of unnumbered generations. We are, therefore, working in harmony with all inherited and psychologic tendencies and reaching an area of the brain that can be developed in no other way. When this door is wholly closed, we must gain access to the intelligence through the other entrances of sight and touch, but if the main door is even slightly ajar, the sensible thing is to squeeze through, and, if possible, pry it more widely open. Wright says:

> There are many children in this situation in our schools for the deaf, and, owing to the lack of sufficient teachers and perhaps also to inadequate appreciation of the possibilities, they are not getting the educational training for their residual hearing that they should have. The medical profession could do much to change this and to induce those in authority to obtain the necessary assistants and do this valuable educative work.

Dr. Kerr Love[5] says that nearly all middle ear disease of later life, both suppurative and nonsuppurative, commences during the earlier years of the school period. He regards the advent of the aural school

5. Love, Kerr: The Aural School Clinique, Glasgow Med. Jour., February, 1916.

clinic as perhaps the most important development which has taken place in the treatment of ear diseases for the last quarter of a century. The author says that not only is treatment more important in the school period than at any subsequent time, but that it is also very successful.

In Glasgow four well equipped school clinics have been in operation for a period of four years. Practically no operative work is undertaken. Cases requiring removal of tonsils and adenoids are referred to the hospital serving the district in which the child resides. During the four years of its existence about 3,250 cases, or 3 per cent. of the children attending school, have been treated. It was found that in most cases permanent arrest of the discharge was effected without operative treatment of any kind. In others attention to the nasopharynx together with careful treatment of the discharging ears was required. The author says that although the results hitherto obtained were very satisfactory, the best results cannot be secured until the school board assumes the whole responsibility for the treatment of the children's ears, including all the necessary surgical measures.

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THE CONDITION OF THE REFLEXES IN POLIOMYELITIS *

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The most constant symptom of poliomyelitis — and the one which should always lead us to think of the possibility of that disease, especially during epidemics — is an alteration in the reflexes accompanying or following a short febrile period.

Various changes in the normal reflex response have been described by numerous investigators, more especially by Wickman, Muller, Zappert, Foerster, Neurath, and recently by Draper, Peabody and Dochez.[1] In studying the large number of cases admitted during the epidemic of 1916 to the Kingston Avenue Hospital, we have encountered some interesting facts to which we shall take the liberty of drawing attention.

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The Condition of the Patellar Reflex.—The knee jerks are the most frequently affected of all reflexes. This is no doubt to be attributed to the common paralytic involvement of the quadriceps extensor group of muscles. In order to show the frequency of alterations in this reflex Table 1 should be instructive, as it has been based on 818 cases of poliomyelitis, most of the patients being admitted in the early paralytic stage. If summarized it will be found that the knee jerks were altered in some way in 81 per cent. of the 818 cases classified.

TABLE 1.—The Condition of the Patellar Reflex in 818 Cases of Poliomyelitis

	Right Knee Jerk	Left Knee Jerk
Absent in	549	538
Diminished in	68	67
Exaggerated in	38	34
Sluggish	9	17
Altered in	664	656
Normal in	154	162
Total cases	818	818

Exaggeration of the Knee Jerks.—Ed. Muller and Wickman[2] have drawn attention to the initial increase, which may precede the onset of paralysis. We have met this change in most all the cases seen early in the preparalytic stage, and we strongly believe it is the usual, if not invariable, change found in the first twenty-four hours of the meningeal phase of the disease. Exaggeration would naturally be expected to precede the later diminution and absence, since it is recognized that the first stage of inflammation is accompanied by increased functional activity, and that this principle applies to the tissues of the nervous system as much as it does to those of any other part of the body. Another factor concerned possibly is that the normal inhibitory influence of the brain through the upper motor neuron is no doubt temporarily diminished by the inflammatory changes which are often present to a certain extent throughout the entire cord.

The reaction is often so marked that the slightest tap with the percussion hammer will elicit a response which will move the foot through an arc of from 30 to 60 degrees. As the preparalytic stage advances this exaggerated response becomes diminished and finally

2. Wickman, Ivan: Nervous and Mental Disease Monograph, Series, No. 16, New York, 1913, p. 48.

disappears when paralysis becomes definitely manifest, and for this reason it often passes unnoticed unless the patient is seen early.

Hyperactivity may, however, persist into the stage of paralysis in a certain proportion of the patients, and most often in those in whom the paralytic involvement is slight. To show the limb or limbs affected and the extent of the paralysis under such circumstances, thirty cases with exaggerated patellar reflexes at this period of the disease have been tabulated in Table 2. When this table is examined two important facts are noticable: (1) the relative infrequence of any marked paralysis in the entire series, and (2) the high proportion of the spastic form of paralysis present. In nearly all the thirty cases classified where the lower limbs were involved the paralysis was slight, for if it had been severe the quadriceps tendon would undoubtedly be affected

TABLE 2.—Degree and Type of Paralysis

Extremity Paralyzed	Total Number of Cases with Affected Extremities	Degree and Type of Paralysis			
		Weak	Partial	Complete	Spastic
Left upper	4	3	..	1	
Both uppers	9	4	2	..	3
Right lower	4	3	1		
Left lower	3	..	1	1	1
Both lowers	15	7	2	..	6
Totals	35	17	6	2	10

to such an extent that an absence of the knee jerk would be the result. Of the thirteen cases in which the upper extremities were concerned, in eight the paralysis was limited to that part of the body, the lower extremities being perfectly normal except for the exaggerated knee jerks. Such cases are extremely interesting and have been previously noted by Wickman,[2] and by Neurath, Zappert, Foerster and Ed. Muller. all of whom are cited by Wickman. Wickman concludes that they are due to a slight injury to the pyramidal tract in its course through the upper regions of the cord.

The large number — ten out of thirty-five — of spastic cases in the series indicates that the meningitic types of poliomyelitis are most apt to be accompanied by hyperactivity of the knee jerks, for spasticity usually belongs to that particular form of the disease.

In three of the thirty cases the knee jerks were entirely absent on the paralyzed side and exaggerated on the opposite or normal side. Wickman, Zappert, Draper and Peabody and Dochez have made an

identical observation in some of their patients. The pathologic basis for this symptom would seem to be that the inflammatory reaction around the cells of the anterior horns on the side with paralysis was sufficiently intense entirely to obliterate the reflex arc, while on the opposite side it was so slight as only to be productive of increased functional activity.

The relative frequence of hyperactivity varied in the different forms of poliomyelitis, as is shown in Table 4, giving, as it does, in percentage ratio, the occurrence of exaggerated, diminished, sluggish and absent reactions. It would tend to prove that an increased response was present most frequently in the meningitic and ataxic cases, and in the

TABLE 3.—Showing the Relation Between the Normal and Altered Reactions—

Type of Poliomyelitis	Right Knee Jerk			
	Normal		Altered	
	Number of Reactions	Relative per Cent.	Number of Reactions	Relative per Cent.
Single Types:				
Myelitic	72	21	267	78
Meningitic	3	23	10	77
Ataxic	20	41	29	59
Bulbar	9	50	9	50
Combined Types:				
Myelitic and meningitic	14	11	111	89
Myelitic and meningitic with hydrocephalus	0	..	13	100
Myelitic, meningitic and bulbar	3	18	14	82
Bulbar and meningitic	0	..	7	100
Bulbar and myelitic	1	5	19	95
Bulbar and myelitic with hydrocephalus	0	..	7	100

combined types of the disease in which meningitic symptoms were present, while it was unusual in the bulbar, bulbar myelitic, and myelitic cases. This last fact differs somewhat from the observations of Wickman and others, who noted that the knee jerks may be exaggerated if the bulb is involved. We think this difference lies in the fact that in the nine cases of our series in which there was an absence of the reflex, the children were mostly in rather poor condition, almost moribund, when examined, and we have only rarely been able to elicit a reaction under such circumstances. In the other nine cases, however, the response was normal, but no doubt had the examination been made in the first twenty-four to forty-eight hours of the disease an exaggeration would probably have been found.

We believe that while the bulbar forms of poliomyelitis may show hyperactivity of the knee jerks in the early meningitic phase, this soon changes to a more or less normal reaction, and later, in the terminal phase, disappears entirely.

Medin[3] noted exaggeration of the patellar reflex in many of the ataxic forms of the disease, but Wickman (p. 75) found a diminished or lost reaction in similar cases. We should be inclined to think with Medin that exaggeration occurs frequently, for we noted this change in 34 per cent. of the total alterations in the ataxic forms of the disease. Wickman (p. 48) has observed cases in which the reflex may be exaggerated in an atrophied and obviously paralyzed leg. Among our

—of the Patellar and Plantar Reflexes in the Various Forms of Poliomyelitis

Left Knee Jerk				Right Plantar				Left Plantar			
Normal		Altered		Normal		Altered		Normal		Altered	
Number of Reactions	Relative per Cent.	Number of Reactions	Relative per Cent.	Number of Reactions	Relative per Cent.	Number of Reactions	Relative per Cent.	Number of Reactions	Relative per Cent.	Number of Reactions	Relative per Cent.
65	19	272	81	144	56	110	43	146	58	106	42
3	23	10	76	5	55	4	44	5	55	4	44
24	45	30	55	33	76	10	23	30	76	9	23
8	44	10	55	11	64	6	35	11	61	7	39
18	14	107	86	56	54	47	45	54	56	42	44
0	..	14	100	5	45	6	54	7	64	4	35
3	17	14	82	5	35	9	64	5	38	8	61
0	..	8	100	6	85	1	14	6	85	1	14
1	4	20	95	10	62	6	37	8	61	5	38
0	..	7	100	1	16	5	83	1	16	5	83

cases we can recall three or four examples of a similar character, and in all the response was markedly increased.

Not infrequently in convalescence the knee jerks were found hyperactive when every other symptom of the disease had disappeared, the patient showing no paralysis of any description and walking in an apparently normal manner. This was probably indicative of the stage of improvement and had succeeded on a diminished or absent reaction, and just preceded the return to normal.

Diminution of the Patellar Reflex.—This often follows the exaggeration of the preparalytic stage, and just precedes the disappearance

3. Medin, O.: Cited by Wickman (Footnote 2), p. 75.

of the reflex with the onset of paralysis. Where the paralytic involvement is slight a diminished response is not infrequent throughout the entire course of the acute stage of the disease. During the stage of improvement it is usually the first change noticed. At times it just precedes the exaggeration which occurs before the reflex becomes normal, but more frequently the change occurs from the diminished to the normal response.

The relative occurrence of a diminished reaction in the paralytic stage varies in the different types of the disease, as is shown in Table 4.

TABLE 4.—Showing the Patellar and Plantar—

Type of Poliomyelitis	Right Knee Jerk				
	Normal	Exaggerated	Diminished	Sluggish	Absent
Single Types:					
Myelitic	72	11	32	4	220
Alterations expressed in per cent.*	..	4	11	1.5	82
Meningitic	3	2	2	1	5
Alterations expressed in per cent.	..	20	20	10	50
Ataxic	20	10	5	..	14
Alterations expressed in per cent.	..	34	17	..	48
Bulbar	9	..	..	..	9
Alterations expressed in per cent.	..	..	..	..	100
Combined Types:					
Myelitic and meningitic	14	12	6	3	90
Alterations expressed in per cent.	..	10.5	5.5	2	82
Myelitic and meningitic with hydrocephalus	..	2	1	..	10
Alterations expressed in per cent.	..	15	7.5	..	77
Myelitic, meningitic and bulbar	3	1	1	..	12
Alterations expressed in per cent.	..	7	7	..	86
Bulbar and meningitic	..	1	1	..	5
Alterations expressed in per cent.	..	14	14	..	71
Bulbar and myelitic	1	..	1	..	18
Alterations expressed in per cent.	..	..	5	..	94
Bulbar and myelitic with hydrocephalus	..	..	..	..	7
Alterations expressed in per cent.	..	..	..	..	100

* The percentages given refer to the different alterations and have no relation to the normal response. This method of expressing the relative frequency of these alterations in percentage was used because the impression is the better conveyed than by figures only.

It is most common in the types in which paralysis is not marked, as would naturally be expected. Thus, of the total alterations it comprised 20 per cent. in the meningitic cases, 17 per cent. in the ataxic, 14 per cent. in the bulbar meningitic, 11 per cent. of the myelitic. That 11 per cent. of the myelitic cases showed a diminished response is to be attributed to the character of the paralysis in these cases, the legs being affected only in a small proportion of this number and, when so, not to any marked extent.

Sluggish Reaction of the Patellar Reflex.—This is the alteration which is encountered with least frequence; it occurs, however, occasionally, and is probably more frequent than our statistical figures would show. This type of reaction is characterized by an unusual slowness and delay in response on percussion over the quadriceps tendon; we do not believe it occurs in one out of every ten meningitic cases, as our figures would tend to indicate, because a classification of only thirteen cases of this type of poliomyelitis is an insufficient number on which to base any hard and fast rules; yet we were con-

—Reflexes in the Various Types of the Disease

Left Knee Jerk					Right Plantar					Left Plantar				
Normal	Exaggerated	Diminished	Sluggish	Absent	Normal	Exaggerated	Diminished	Sluggish	Absent.	Normal	Exaggerated	Diminished	Sluggish	Absent
65	10	30	4	228	144	6	16	3	85	146	4	18	3	81
..	3.5	9	1.5	84	..	5.5	14	2.5	77	..	3	17	25	76
3	2	2	1	5	5	2	..	..	2	5	2	..	..	2
..	20	20	10	50	..	50	..	..	50	..	50	..	..	50
24	9	7	..	14	33	3	4	..	3	30	2	5	..	2
..	30	23	..	47	..	30	40	..	30	..	22	55	..	22
8	..	..	..	10	11	..	..	..	6	11	..	..	..	7
..	..	..	..	100	..	..	..	..	100	..	..	..	..	100
18	11	7	3	86	56	3	9	..	35	54	2	10	..	30
..	10	6.5	2.5	80	..	6	19	..	74	..	4	23	..	72
..	2	1	..	11	5	1	..	..	5	7	1	..	..	3
..	14	7	..	78	..	16	..	..	83	..	25	..	..	75
3	1	1	..	12	5	1	1	..	7	5	1	1	..	6
..	7	7	..	86	..	11	11	..	77	..	12	12	..	75
..	2	1	..	5	6	..	..	..	1	6	..	..	..	1
..	25	12	..	62	..	..	..	..	100	..	..	..	..	100
1	..	1	..	19	10	..	..	..	6	8	..	..	1	4
..	..	5	..	95	..	..	..	..	100	..	..	..	20	80
..	..	..	..	7	1	..	..	..	5	1	..	..	..	5
..	..	..	..	100	..	..	..	..	100	..	..	..	..	100

vinced of its relative frequence where marked meningitic symptoms were present.

There was a peculiar variety of sluggish reaction which was occasionally encountered. In such instances it was necessary to percuss the patellar tendon several times before a response was obtained, and when elicited this latter was often of an exaggerated character. There appeared to be necessary a summation of impulses before the threshold of inhibition could be passed and a reaction obtained. The inflamed condition of the neuroglia tissue may account for the hyperactivity, after the threshold of inhibition was overcome.

Absence of the Patellar Reflex.—Wickman states in his monograph (p. 48) that "absence of the knee jerk is the rule."

Certainly the percentage of this alteration as compared with the percentage of other changes (Table 4) would amply justify this statement. In the purely myelitic and in the combined myelitic types, it comprised from 71 to 100 per cent. of the changes found; in bulbar types from 86 to 100 per cent. of the total alterations, while in the meningitic and ataxic forms it represented only 59 per cent. of the entire changes. These statistical findings are about what clinical observation would lead one to conclude, because it is the quadriceps group of muscles which seem remarkably prone to affection, and where the paralysis is at all marked the reflex response disappears.

"The loss of the patellar reflex may be the only demonstrable objective sign of the disease," according to Wickman, Ed. Muller and Zappert. We have encountered similar cases in which there was present only an absence of the knee jerk, and yet the spinal fluid and the history both pointed decidedly to Heine-Medin's disease. Necessarily, it is difficult to base a diagnosis on such an alteration, and it is only when an epidemic is prevalent that abortive cases of this kind are apt to be considered suspicious enough to justify the procedure of lumbar puncture. That they may occur, however, is well established, and their importance lies in the fact that although usually unrecognized they are just as dangerous in spreading the contagion of the disease as the frankly paralyzed patients.

Normal Reaction of the Patellar Reflex.—The knee jerks may remain normal throughout the paralytic phase of the disease. The bulbar and ataxic cases most commonly exhibit a normal response, representing 50 per cent. of the reflex reactions in the former and 41 per cent. in the latter (Table 3). These figures are not surprising, for paralytic involvement of the lower limbs is a negative quantity in both types. The occurrence of a normal response in 21 per cent. of the myelitic cases is to be attributed to the limitation of the paralysis in these cases to the upper extremities and trunk. It is interesting to note that in the forms of the disease in which the hydrocephalus was most marked there was a total absence of the normal response, the reflexes being altered in 100 per cent. of the cases.

The Condition of the Plantar Reflex.—The plantar reflex has been selected to show the changes that the superficial reflexes undergo, just as the patellar reflex was described to bring out the alterations occurring in the deep reflexes.

In the preparalytic stage: The plantar reflexes are exaggerated in the early part of this stage, but in a somewhat dissimilar manner to the changes that occur in the knee jerks at about the same period. The

type of reaction elicited is a peculiar example of hyperactivity, in that it probably involves mostly the sensory side of the reflex arc, and concerns a more extensive muscular response than that of a mere downward flexion of the toes. No doubt the hyperesthetic condition of the skin is the factor most concerned in producing the exaggerated response. Under normal conditions stroking the sole of the foot produces a slight flexion of the toes. In the preparalytic stage of poliomyelitis this same stimulus causes the child quickly to pull the foot out of reach of further irritation by flexing the leg on the thigh and semi-flexing the thigh on the abdomen at the same time that the toes are plantar flexed.

In the paralytic stage: The reaction rapidly changes as the disease advances and becomes normal, diminished or lost by the time paralysis appears. Table 5 gives the condition of the reflex in over 600 cases in which most all of the patients were examined in the early paralytic stage.

TABLE 5.—Condition of the Plantar Reflex in the Early Paralytic Stage

	Right Plantar	Left Plantar
Absent	194	184
Diminished	44	50
Sluggish	6	7
Exaggerated	17	17
Altered in	261	258
Normal in	382	369
Specified in	643	627

If the figures in Table 5 are considered on a percentage basis we find that alterations were present in only 41 per cent. of the series, quite different from the condition of the knee jerks previously mentioned (Table 1), which were found altered in 81 per cent. of over 800 cases. This difference is to be attributed certainly to the fact that the plantar flexors of the toes and foot are affected much less frequently than the quadriceps group of muscles.

The relative frequence of the various alterations in the different types of the disease are given in Table 4. An exaggeration of the reflex may persist into the paralytic stage, most especially in the meningitic and ataxic cases. A diminished response was most common in the ataxic, the myelitic meningitic and the purely myelitic cases. An absence of reaction was most frequent in the purely bulbar, the combined bulbar and the myeletic types, and least frequent in the meningitic and ataxic forms.

The percentage of normal to altered reactions (Table 3) in the various forms of the disease was such that a normal response was most

common in the ataxic, bulbar, bulbar myelitic and bulbar meningitic cases.

There is more or less of a constant relation between the degree of paralysis and the presence or absence of the plantar reflex, in that when the paralytic involvement of the lower extremities is slight or partial the reflex is only occasionally missing, while when the paralysis is complete absence is the rule. In this last class of cases often the first sign of improvement is the gradual reappearance of the plantar reflex, the reaction being diminished at first, but slowly becoming normal again as the paralysis diminishes.

In cases of Heine-Medin's disease in which the polyneuritis is marked, it is easy to be deceived as to the actual extent of paralysis, especially so because one hesitates to employ passive motion of the lower limbs for this purpose, owing to the severe pain produced thereby. To avoid this the physician may be led to substitute repeated stimulations of the soles of the feet as in eliciting a plantar reflex, which would ordinarily result in the child's pulling the foot and leg, if not paralyzed, away from further irritation. But the neuritic affection renders all movement so much to be feared that the little patient will rather submit to the irritation than to move his foot or leg away, despite the fact that the degree of paralysis would in no way interfere with the motion necessary.

Ker[4] says the plantar reflex is frequently absent in epidemic meningitis. In the meningeal form of poliomyelitis we have found it absent in only 22 per cent. of the cases. From a differential standpoint, therefore, it is probably more frequently absent in epidemic meningitis than in the meningeal form of poliomyelitis.

Babinski Sign.—The pathologic alteration of the plantar reflex which is called the Babinski sign we have encountered only rarely in poliomyelitis during the paralytic stage, even in the meningeal form of the disease. Foerster,[5] however, has found it present on either one or both sides in all cases; it was not continuously demonstrable, but disappeared occasionally only to return. Wickman (p. 49) says merely that it has been observed.

In 1,017 cases terminated at the Kingston Avenue Hospital, it was encountered only 9 times in patients over 2 years of age. Kernig's sign was present in all the 9 cases; the knee jerks were absent in 5, diminished in 2, exaggerated in 1, sluggish in 1.

The type of the disease in these 9 cases was meningitic 2, bulbar myelitic meningitic 4, and meningitic myelitic 3.

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4. Ker, C. Buchanan: Infectious Diseases, London, 1909, p. 494.
5. Foerster, O.: Cited by Wickman (Footnote 2), p. 49.

Babinski's sign is quite common in tuberculous meningitis (Koplik[6] found it present in twenty-three out of fifty-two cases examined). It is not quite so frequent, but occurs in a minor percentage of cases of meningococcus meningitis. Hence its presence in a case in which the diagnosis is in question would be a point decidedly in favor of either of these diseases, especially the former, and against poliomyelitis.

The patients with poliomyelitis in which the Babinski phenomenon was found present never exhibited so marked and persistent a reaction as that seen in tuberculous meningitis.

Kernig's Sign.—In the paralytic stage we have encountered two types of response to the movements employed in testing for Kernig's sign—one, the true reaction, the other the "pseudoreaction." They are easily confused, and while the true reaction occurs only occasionally, and when so is limited to the meningitic forms of the disease, the pseudoreaction is very commonly present in cases exhibiting a moderate or severe degree of polyneuritis.

As in other forms of meningitis, the true response is characterized by a true spasm of the hamstring muscles when the thigh is semiflexed on the abdomen and an attempt is made to extend the leg on the thigh. The pseudoresponse, on the contrary, is associated with a voluntary resistance of the hamstring muscles in an effort on the part of the child to prevent further extension of the leg, owing to the pain produced. It is an analogous sign to that of Lasigne, so commonly encountered in sciatica, and the pathologic basis would seem to be somewhat similar, namely, a neuritis of the nerve trunks of the leg and thigh, the stretching of which causes intense pain. The reflex muscular spasm is lacking in these cases, and there is distinct pain on pressure over the posterior tibial nerve in the calf of the leg, over the sciatic nerve at the upper margin of the popliteal space and in the middle of the posterior aspect of the thigh.

In twenty meningeal cases Kernig's sign was mentioned as present in sixteen and was not specified in four. Statistically, it is also mentioned frequently in the combined myelitic meningitic forms of the disease, but it was a question in such cases whether to attribute it to a meningeal reaction or to a polyneuritic affection of the nerves, as often no distinction seems to have been drawn between the two.

Ankle Clonus.—Wickman and also Neurath found an ankle clonus present in cases in which an increase of the leg reflexes coexisted with a flaccid paralysis of the arm of the same side or with a lesion at a still higher level.

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6. Koplik, H.: Tuberculous Meningitis, Osler and McCrae's System of Medicine, 1913, p. 422.

Foerster[5] found a clonus in the very accute stage of the malady.

Just as in the case of Kernig's sign we had noted a true reaction and a pseudoreaction, so a similar observation was made in regard to the response obtained when passive movements were employed to determine the presence or absence of ankle clonus.

A true response was found very rare in poliomyelitis, occurring only in 6 of the 1,017 cases terminated. In these 6 cases, the type of the disease was distributed as follows: 2 were purely meningitic; 2 myelitic meningitic, 1 myelitic with facial involvement, 1 myelitic meningitic and bulbar. The paralysis was spastic in 2, and flaccid in 4. In the spastic cases both upper and lower limbs were involved; in the flaccid cases only the lower limbs. The knee jerks were exaggerated in 2 cases and absent in 3. Babinski's sign was present concomitant in 3 of the 6 cases.

A true ankle clonus is so rare in poliomyelitis as compared to the various forms of meningitis that if present in a case in which a diagnosis is in question, it would always be a point decidedly against the former disease.

The pseudoreaction is, however, frequent where polyneuritis is present, and may simulate slightly a true response; but the repeated spasmodic muscular contractions of the tendo achilles are absent and instead there is a marked voluntary resistance to the dorsal flexion of the foot, and at the same time the child screams with an intense pain which radiates up along the nerve trunks of the leg and thigh. We think that the pathologic basis for a reaction of this kind is the neuritic affection of the nerve trunks of the lower extremities, and have always found it a more or less constant evidence of the presence of the polyneuritis.

The Pupillary Reflex.—This is altered but little if at all during the acute stage of the malady. It may be slightly sluggish in cases with marked hydrocephalus, but a reaction is always present except in moribund cases. Thus, in 447 patients in which a reflex was mentioned, it was normal in 424, sluggish in 14, absent in 9. These latter 9 cases were of bulbar type, in a more or less moribund condition when examined, and no doubt the absence of the reflex was due mostly to the moribund state of the patients. We have not observed unequal degrees of reaction in the two eyes in any true case of poliomyelitis.

Patients were occasionally encountered in whom the pupils were of unequal size and in whom the reaction to light differed on either side, but a diagnosis of tuberculous or purulent meningitis was ultimately made in all such instances, either from the examination of the spinal fluid or the findings at necropsy. The pupillary reflex was tested mostly as regards light, and only occasionally as to accommodation, for,

so young were most of our patients that it was usually difficult accurately to test the reflex in this latter respect.

The Patellar Reflex in the Paralyzed as Compared to the Nonparalyzed Extremity.—In cases in which the paralytic involvement was limited to one leg, it was interesting to note the condition of the knee jerks in the affected as compared to the unaffected extremity. Draper, Peabody and Dochez[1] found the reflex present more often than absent on the healthy side. Our findings have been somewhat similar. Thus, of 23 cases (Table 6) in which the right leg alone was paralyzed, the right knee jerk was absent in 15, normal in 4, exaggerated in 1, diminished in 1; while the left knee jerk was absent in 6, normal in 13. exaggerated in 1, diminished in 3. In 28 cases in which the left leg alone was paralyzed, the patellar reflex on the right side was normal in 11, exaggerated in 2, diminished in 2, sluggish in 2, absent in 11; on the left side it was normal in 5, exaggerated in 1, diminished in 2, sluggish in 2, and absent in 18.

TABLE 6.—THE PATELLAR REFLEX WHEN ONLY ONE LEG WAS PARALYZED

Alterations	Right Leg Paralyzed		Left Leg Paralyzed	
	Right Knee Jerk	Left Knee Jerk	Right Knee Jerk	Left Knee Jerk
Normal	4	13	11	5
Exaggerated	1	1	2	1
Diminished	3	3	2	2
Sluggish	..	..	2	2
Absent	15	6	11	18
Specified in	23	23	28	28

TABLE 7.—THE CONDITION OF THE PATELLAR REFLEXES WHEN THE PARALYSIS WAS LIMITED TO THE FACIAL NERVE

Alterations	Right Facial		Left Facial	
	Right Knee Jerk	Left Knee Jerk	Right Knee Jerk	Left Knee Jerk
Normal	7	8	14	14
Sluggish	1	1	1	1
Diminished	1	1	1	1
Absent	6	5	3	3
Mentioned in	15	15	19	19

The Condition of the Patellar Reflexes When the Paralysis Was Limited to the Upper One Half of the Body.—In 11 similar cases Draper, Peabody and Dochez found the knee jerks were present on both sides 5 times and absent 6 times. In 19 of our cases the condition of the patellar reflexes was as follows: Absent in 9 cases, diminished in 1, exaggerated in 2, and normal in 7. Such figures agree essentially with those of the authors heretofore mentioned. We noted, however, that when the paralysis was limited to one upper extremity, the knee jerks were only exceptionally absent.

The Patellar Reflexes When the Facial Nerve Alone Was Paralyzed.—In 15 cases of right facial paralysis the knee jerks were absent on the right side in 6, and on the left side in 5. In 19 cases of left facial paralysis they were absent in both legs in only 3. These figures would appear to indicate that the knee jerks may be lost in between 16 and 30 per cent. of cases of facial paralysis. The plantar reflexes remained unaltered in all instances.

SUMMARY

1. The most common symptom of poliomyelitis is an alteration in the reflexes accompanying or following a short febrile period.

2. The patellar reflex is most frequently affected owing to the common involvement of that region of the spinal cord which innervates the quadriceps extensor group of muscles. It was altered in various ways in 81 per cent. of 818 cases.

3. Hyperactivity of the knee jerks is usually, if not invariably, the first change to occur in the preparalytic stage. It may be so marked that the slightest tap with the percussion hammer will elicit a response which will cause the foot to move through an arc of from 30 to 60 degrees. The reflex, as a rule, becomes diminished and finally absent as paralysis supervenes, but it may persist exaggerated in cases in which the paralytic involvement is slight, and in which the lower extremities are not concerned to any marked extent, as well as in cases that are of the spastic variety. It may also be met with where the paralysis is limited to the upper half of the body. In rare cases there may be encountered an absence of the knee jerk on the paralyzed side and an exaggeration on the opposite and healthy side.

4. Hyperactivity of the patellar reflex is most frequent in the meningitic and ataxic cases, and in the combined types of the disease in which meningitic symptoms were prominent. Absent or normal response is the rule in purely bulbar cases, except in the very early stages.

5. An exaggerated reflex may be encountered in an atrophied and obviously paralyzed leg.

6. Not infrequently the knee jerks are found hyperactive in convalescence when every other symptom of the disease has disappeared, no doubt indicative of the stage of improvement and just preceding the return to normal.

7. A diminished patellar reflex usually precedes its disappearance with the advent of paralysis. It may persist, however, during the entire course of the acute stage, in cases with slight paralysis, especially of the meningitic and ataxic types. During the stage of improvement it is, as a rule, the first change noticed.

8. A sluggish patellar reflex is rather unusual, except in the meningeal forms of the disease. Very rarely sluggish but hyperactive reflexes are encountered.

9. Absence of the knee jerk is the most common alteration, and it is most frequently encountered in the myelitic and bulbar types of the malady. This symptom may be the only demonstrable objective sign of the disease, according to Wickman, Ed. Muller and Zappert.

10. The patellar reflex may remain normal throughout the entire paralytic phase, especially in bulbar and ataxic cases. It is also common in myelitic cases when the paralysis is limited to the upper extremities and trunk. It is scarcely ever encountered where the hydrocephalus is at all marked.

11. The plantar reflexes are exaggerated in the preparalytic stage. This hyperactivity is of a peculiar type and is accompanied by a response which comprises not only a movement of the foot, but also of the entire leg. The reflex was alterated in only 41 per cent. of 643 cases specified in the paralytic stage. An exaggerated response may persist into the paralytic stage, more especially in the meningitic and ataxic classes of cases. A diminished reaction was found most common in the ataxic, the myelitic meningitic, and the purely myelitic forms of the disease. The reflex was absent most frequently in the purely bulbar and in the combined bulbar and myelitic cases. A normal reaction was encountered most often in the ataxic, bulbar myelitic and bulbar meningitic forms of the malady. Often the first sign of improvement in cases with marked paralytic involvement is the gradual reappearance of the reflex.

12. There is to be noted two types of response to the movements employed in testing for Kernig's sign, the true reaction, the other, the "pseudoreaction" or false reaction. The true reaction is only occasionally met with, and is limited to those forms of the disease in which meningitic symptoms are extremely prominent. The pseudoreaction is common in all cases exhibiting a moderate or severe degree of polyneuritis, and is associated with voluntary resistance to extension

of the leg on the thigh, owing to the pain thereby produced. It is an analogue sign to that of Lasigne, so frequent in sciatica.

13. The Babinski phenomenon is relatively rare in poliomyelitis, but it occasionally occurs in the meningitic form of the disease. Its presence in a case in which the diagnosis was doubtful would always be decidedly in favor of tuberculous, and, to a less extent, cerebrospinal meningitis.

14. A true ankle clonus is likewise very rare in contradistinction to the other forms of meningitis. The reaction may be simulated in cases in which the polyneuritis is marked, owing to the severe pain caused by the movements employed.

15. The pupillary reflex is but little altered. It may be slightly sluggish in cases with marked hydrocephalus and during the very early stage; but a reaction is almost always present except in the moribund stage.

16. When paralysis is limited to one leg only, the knee jerks on the healthy side are more often present than absent. Also when the upper extremities are alone involved the patellar reflexes are more often present than absent. In a minor percentage of cases of facial nerve paralysis the knee jerks may be lost.

INFANTILE SCURVY

V. A STUDY OF ITS PATHOGENESIS *

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For some years we have been studying various aspects of the symptomatology and dietetics of infantile scurvy. In a recent paper[1] it was shown that pasteurized milk brings about this disorder in some cases unless an antiscorbutic food is included in the dietary. The type of scurvy induced under these conditions, as noted elsewhere, is not the textbook variety of this disease, but what has been termed latent or subacute scurvy, characterized by anemia and pallor, failure to gain in weight, rapidity of pulse and respiration, tenderness of the bones, and by a sharp recession of all these signs and symptoms when orange juice or other antiscorbutic foodstuff is given. In asserting that scurvy is brought about by pasteurized milk it should be emphasized that this is not synonymous with saying that this disorder is caused by heating the milk to the temperature of pasteurization. It is for this reason that we have, in this connection, referred to pasteurized milk rather than to pasteurization, as the former term includes not only the heating process, but the handling, subsequent cooling, aging and other factors.[2]

Some have questioned whether pasteurized milk is really involved in the production of scurvy. The fact, however, that when one gives a group of infants this food for a period of about six months, instances of scurvy occur, and that a cure is brought about when raw milk is substituted, taken in conjunction with the fact that if we feed the same number of infants on raw milk, cases of scurvy will not develop—these results seem sufficient to warrant the deduction that pasteurized milk is a causative factor. The experience in Berlin, noted by Neumann[3] and others, is most illuminating and convincing in this connection. In 1901 a large dairy in that city established a pasteurizing plant in which all milk was raised to a temperature of about 60 C. After an interval of some months infantile scurvy was reported from various sources throughout the city. Neumann[3] writes about the situation as follows:

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* Submitted for publication Sept. 7, 1917.

1. Hess, A. F.: Jour. Am. Med. Assn., 1917, **68**, 239.

2. In the article[1] referred to above on "Subacute and Latent Infantile Scurvy" this point was brought out as follows: "In referring to pasteurized milk as inducing scurvy I do not wish to state that the heating is necessarily altogether responsible for the result. There may well be other contributory factors, such as the staleness of the milk."

3. Neumann, H.: Deutsch. Klin., 1904, **7**, 341.

"Whereas Heubner, Cassel and myself had seen only thirty-two cases of scurvy from 1896 to 1900, the number of cases suddenly rose from the year 1901, so that the same observers — not to mention a great many others — treated eighty-three cases in 1901 and 1902." An investigation was made as to the cause, and the pasteurization was discontinued. The result was that the number of cases decreased just as suddenly as they had increased. It should be added that the milk was also brought to the boiling point in the home, as is the custom throughout Germany.

For two years the milk which we used at the infant asylum was pasteurized commercially at 165 F. for thirty minutes; for two subsequent years the dealers raised it to a temperature of only 145 F. for thirty minutes. According to our experience, milk heated to the higher degree of temperature induces scurvy more readily than that which is brought to only 145, judging by the results of the four-year period. During the past year we have bought raw certified milk, the best milk which is sold in the city, and pasteurized it in the institution at 145 for thirty minutes. Various formulas were prepared with this milk, so that should any disorder develop we might be in a position to analyze the trouble and correct the dietary defect. Among six infants given milk which was pasteurized and prepared for feeding on the morning it was received, none developed scurvy. One infant in our institution which had been receiving commercially pasteurized milk for many months and which showed symptoms of subacute scurvy improved on this home pasteurized milk. It may be said, therefore, that this milk manifested almost no tendency to produce scurvy. How, then, did it differ from the commercially pasteurized milk which we had previously been buying? It differed mainly, as far as we can judge, in the interval which elapsed between the heating process and the consumption of the milk. In New York City the major portion of the bottled milk is Grade B, most of which is pasteurized after it reaches the city, soon after midnight; fully two-thirds of this milk is delivered to the consumer the same morning on which it is pasteurized; however, part of it is held over and delivered twenty-four hours later. The better milk, Grade A, is largely pasteurized in the country, so that an interval of twenty-four hours elapses between the heating and delivery.[4] In order to reproduce these conditions, we held over some of the pasteurized milk for twenty-four hours on ice, so that it corresponded more closely to Grade A milk. Of eight infants who received formulas made with

4. We found that as a matter of fact the interval following pasteurization was forty-eight hours in milk which we received and which had been pasteurized at the creamery. The milk was stored by the dealers for twenty-four hours in the city, so as to provide a constant supply in case of delay or failure of delivery from the country.

this type of milk (Pasteurized II) two showed scorbutic signs which promptly yielded to orange juice. In one of them the onset seemed to have been precipitated by an intercurrent infection of "grippe." Although these results point to the influence of the freshness or staleness of pasteurized milk, they likewise indicate that aging must be considered only a mild scorbutic agent. This deduction is forced on us by the mild nature of the scorbutic process, by the paucity of cases developing, and by the further observation that among eight other infants who were given the milk which had been kept on the ice for forty-eight hours following pasteurization (Pasteurized III), only two evinced symptoms of subacute scurvy. That aging affects raw milk similarly was shown by the fact that one baby developed latent scurvy among a group of four who were receiving Raw III milk, that is, certified milk which was kept for forty-eight hours on the ice before preparing the formula. This infant developed an eczematous skin condition, to which we have drawn attention before, and which we have frequently noted in association with scurvy. When orange juice was given the skin lesions disappeared, the general condition improved, and there was a marked gain in weight.

That the degree of heat to which the milk is subjected is not an all important factor in rendering the dietary unsuitable was clearly shown in the cases of some infants that received milk which had been boiled for a period of five minutes. After an interval of five months one well nourished infant, 11 months of age and weighing 18½ pounds, showed pallor, some periosteal tenderness, slight peridental hemorrhage and a rapid pulse. These symptoms were alleviated by a substitution of raw milk. It is furthermore evident from the reports of others that boiled milk cannot be an important etiologic factor in bringing about a scorbutic condition. When we consider the thousands of infants that receive milk of this kind and thrive, and that a moderate number must be deprived of orange juice or other antiscorbutic food, we must realize that boiled milk can lead to scurvy only in a mild degree. Statistics such as those of Variot,[5] who has distributed in his out-patient department during a period of twelve years 400,000 quarts of sterilized milk (heated in the half liter bottles and hermetically sealed at the farm) without observing a case of scurvy, must be accorded weight in this connection. It is to be noted, however, that Variot remarks that these infants frequently develop anemia unless additional diet is given, so that it must be considered open to question whether careful and repeated examinations (such as can be carried out only at home or in an institution) might not have uncovered some of the minor manifestations of scurvy. Of course, unless it is certain

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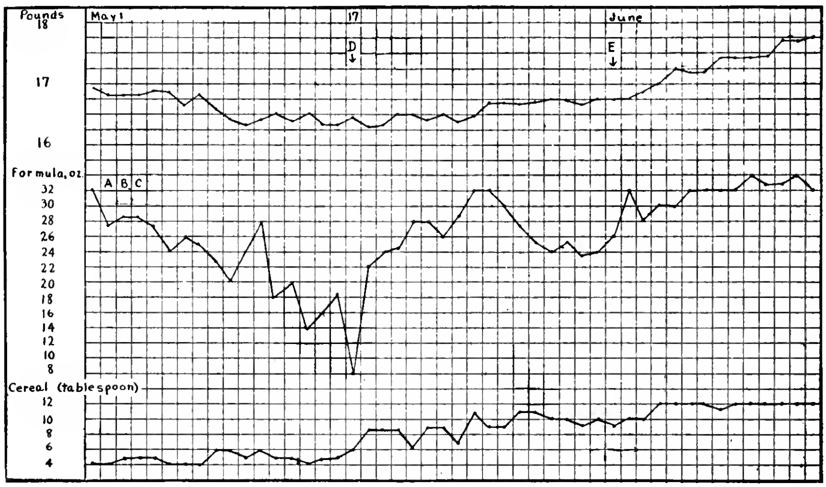
5. Variot, G.: Compt. rend. de l'Acad. d. sc., 1905, **139**, 1002.

that these infants were receiving only sterilized milk, and absolutely no other food, for a period of at least six months, they cannot be considered as affording a test of the question.

Four infants were given the milk for forty-eight hours after it had been boiled, and in one instance inconclusive signs of scurvy developed. That aging, however, may also play a rôle in relation to the use of sterilized milk is well illustrated by some cases in the literature where babies developed scurvy on sterilized milk which had been sent to the country, and where they recovered on receiving the same milk freshly sterilized. In some of these instances the milk was some weeks old. There is a point, one which is lost sight of, which should be emphasized



Joseph G., aged 9 months. Chart showing stationary weight in spite of marked variation of fluid intake (due to oliguria followed by diuresis). A = Schloss milk; B = cod liver oil; C = egg yolk; D = 1 ounce of orange juice; E = potato (orange juice stopped).

in connection with a discussion of the rôle of heated milk in the causation of scurvy. It is taken for granted that if pasteurization will induce scurvy, heating the milk to a still higher degree will certainly lead to this more surely and constantly. This deduction is by no means warranted. Indeed, from personal experience, it would seem that *milk which has been boiled is less apt to induce scurvy than milk which has been pasteurized,* heated to 165 or a lower temperature. This was well illustrated by putting four infants, who were receiving freshly pasteurized milk, on "evaporated milk," so-called because in the course of heating for five to six hours it had been reduced to one-quarter its volume. It thus resembled in many respects the evaporated milk to be bought in the market. In preparing the formulas for these infants

due cognizance was taken of the concentration of fat, sugar and proteins of the milk. This food was well taken by the babies, and after a period of five months none manifested signs of scurvy.

As it has been claimed that scurvy is an acidosis, brought about by a long continued diet of high acidity, the reaction of the various diets was recorded. This is given in Table 1. It will be seen that pasteurized milk does not increase in acidity during the first twenty-four hours, and but little after forty-eight hours. Schloss milk, which is very prone to induce scurvy, has a very low acidity. Evidently the answer does not lie in this direction. It is probable that pasteurized milk

TABLE 1.—Acidity of the Various Milk Preparations Used

Type of Milk	Age, Hours	Number of Cubic Centimeters of Tenth-Normal Sodium Hydroxid Required to Neutralize 100 C.c. Milk							
		April 13	April 14	April 16	April 17	April 18	April 19	April 20	April 21
Raw.................	Fresh	14.9	14.1	16.9	18	18	17	17	18
Sterilized............	Fresh	15.1	14.2	16.3	16	16	19	18	19
Sterilized (III).......	48	16.0	16.4	16.5	23	21	21	23	20
Pasteurized (I)......	Fresh	17.3	15.3	17.9	18	18	19	16	18
Pasteurized (II).....	24	17.5	15.7	17.3	17	17	18	18	20
Pasteurized (III)....	48	20.1	17.3	17.7	19	20	20	18	22
Pasteurized (III)....	72*	16.6	23.2	17.0	18	27	19	21	24
Pasteurized (II) with flour†.........	24	....	....	....	..	13	13	14	16
Pasteurized (III) with flour†.........	48	....	....	....	13	36	14	19	16
Evaporated milk....	24	....	....	....	..	..	29	21	21
Schloss milk.........	Fresh	8.4	6.4	8.7	6	7	7	6	12
Albumin milk........	Fresh	26.4	28.6	41.4	40	46	34	39	49

* Last bottle of pasteurized III formula given on the following morning.
† Formula of two-thirds milk, one-third barley water, with 3 per cent. cane sugar.

constitutes quite a different medium for the growth of bacteria than raw milk, and that it may favor the development of gas-forming or other types of bacteria.

In view of the fact that it has been stated by Braddon and Cooper,[6] in connection with beriberi, that there is a definite relationship between the amount of carbohydrate in the diet and the occurrence of this disorder, for example, that when the carbohydrate is doubled, the rate of onset of beriberi is increased proportionately, it seemed worth while to observe whether this relationship obtained for scurvy. Accordingly, 3 per cent. of flour was added to the diet of four infants which were

6. Braddon, W. L., and Cooper, E. A.: Brit. Med. Jour., June 20, 1915.

receiving the usual mixture of freshly pasteurized milk and barley water. In this way a milk food was prepared similar to some of the commonly used proprietary foods.[7] No noticeable effect was observed —certainly no result which could be interpreted as indicating the existence of a biologic law such as Braddon and Cooper have formulated for beriberi, which presupposes that carbohydrate requires a proportionate amount of "vitamin" for its metabolism in the body. On the other hand, the proprietary foods, composed of carbohydrates, which are stale and have been subjected to a high degree of heat, do seem to lead to scurvy.

From the foregoing it would seem clear that the preparation and condition of the milk may lead to the development of infantile scurvy. It is equally evident, however, that the milk cannot be the sole or determining etiologic factor. The mere fact that only a few of the infants developed signs of this disorder under the various dietaries is convincing evidence of the participation of one or more additional causative agents. There is, indeed, no dietary of which it can be stated that it is certain to produce scurvy, no single food preparation of which we can postulate that, provided it is taken for a sufficiently long period of time, scurvy will certainly manifest itself. The nearest approach to this situation occurs when Keller's "malt soup" is fed to infants. It can be confidently stated that if infants are fed with this mixture of malt, flour, milk, potassium carbonate and water for five to six months, especially if pasteurized milk is used, the majority will evince definite signs of scurvy. Greatly to our surprise, we experienced this result a few years ago while we were using pasteurized milk. The fact that the disorder comes about more readily when pasteurized milk is employed, gives weight to the opinion of Neumann that the heating of milk for a second time lends it scorbutic qualities. We wish, however, to qualify his statement by adding that this seems to be true only if there is an interval between the two heating processes. If one pasteurizes the milk, allows it to cool, and then immediately brings it to the boiling point, the twofold heating does not produce the same deleterious effect.

As is well known, scurvy, infantile scurvy, beriberi, pellagra, rickets, and some other diseases have been linked together into one group; it is evident that there are symptomatic and pathologic similarities among these diseases sufficient to render it profitable to group them together. In recent papers we have drawn attention to common symptoms in infantile scurvy and beriberi, such as cardiac enlargement and tachycardia, and others have brought out points of resemblance between

7. The flour was cooked with the barley water and sugar and added to the pasteurized milk.

members of this group. The basis of the classification, however, is etiologic rather than symptomatic, and is founded on the assumption that they all are nutritional or rather dietary diseases. Although there has been an increasing tendency to admit their similarity and even their dietary nature, two totally different conceptions of their pathogenesis are current. One school regards them purely as "deficiency diseases," whereas the other believes that they are of toxic origin. Some twenty years ago Eijkmann,[8] in a paper which has become classic, described a polyneuritis which he was able to produce in fowl and which closely resembled the beriberi of man. He attributed this disorder to a toxin found in the intestinal canal, and many subsequent investigators, repeating or enlarging on his experiments, expressed themselves of the same mind. Kohlbruegge[9] was the first, however, to suggest a grouping of these diseases, designating them by the name of "fermentative diseases" and asserting that they were due to poisons which were formed by harmful bacteria which had gained predominance in the intestinal canal. Very recently Williams,[10] after many years of work in this field, has also come to the conclusion that this group of diseases is of toxic origin. On the other hand, an entirely different conception has been in vogue for the past few years, mainly due to the writings of Funk.[11] This conceives of these disorders as being due entirely to a lack of essential food substances, the "vitamins"— as being essentially deficiency diseases. A division of opinion similar to that which exists regarding the etiology of this entire group of diseases, and as to beriberi in particular, exists in regard to the pathogenesis of infantile scurvy. Barlow took the point of view that it was brought about by a diet which had been deprived of some of its essential constituents. The excellent report of the American Pediatric Society[12] cautiously refrained from expressing a decided opinion on this point, merely declaring that "the development of the disease follows in each case the prolonged employment of some diet, unsuitable to the individual child." An interesting minority report of this committee signed by Caillé, however, rendered the opinion that it is "a chronic ptomain poisoning due to the absorption of toxins." Neumann,[3] one of the most thoughtful observers and students of infantile scurvy, also regarded it as "a chronic poisoning." Hart,[13] who drew his conclusions mainly from experiments on monkeys, characterizes it as a "dyspeptic intoxication." Nevertheless, the literature contains many articles which accept Funk's

8. Eijkmann, C.: Virchows Arch. f. path. Anat., 1897, p. 253.
9. Kohlbruegge, J.: Centralbl. f. Bakteriol., Orig., 1911, **60,** 223.
10. Williams, R. R.: Am. Med., November, 1916, p. 756.
11. Funk, C.: Die Vitamine. J. F. Bergmann, Wiesbaden, 1914.
12. Rep. Am. Pediatric Soc.: Arch. Pediat., July, 1898, p. 481.
13. Hart, C.: Jahrb. f. Kinderh., 1912, **76,** 507.

point of view in its entirety and agree that we are dealing with a pure "deficiency disease."

A feature which has forced itself on the attention of many who have written on the subject is the multiplicity and variety of the foods which may bring about scurvy in the infant. Pasteurized milk, milk containing a high fat percentage, buttermilk containing but little fat, albumin milk containing much protein, and the proprietary foods rich in starches, are among the varied and incongruous number. It is of course possible that these dietaries, however different they may seem, may all be lacking a common chemical constituent. What tends strongly against this point of view is the fact, already mentioned, that with none of these dietaries can scurvy be brought about with regularity. This lack of reaction between cause and effect must lead us to conclude that the deficiency cannot be the sole cause; indeed, that it does not act directly in bringing about the disorder.

In order to gain a clearer idea as to the possible nature of the etiologic factors it will be well to turn back and consider the nature of the symptoms and pathologic changes of infantile scurvy. In the first place it should be remembered that we have signs of nerve involvement. These comprise cardiorespiratory phenomena, clearly indicating involvement of the pneumogastric nerves, occasionally changes visible in the optic disks, abnormalities of the deep reflexes, and probably sensory disturbances. The symptoms and changes common to this group of diseases, therefore, resemble those brought about by poisons of various kinds — the cottonseed poisoning in swine,[14] the toxic products of the wheat embryo,[15] or even mineral poisons such as mercurial poisoning in man.[16] The nervous symptoms, especially the irritability of the heart, may be compared to those of the enterogenous intoxication or enterotoxic polyneuritis described by Von Noorden.[17] The experiments of Abderhalden and Lampe[18] lend weight to the view of the formation of a toxin in the intestinal tract in this disorder. These investigators were able to bring about polyneuritis in pigeons and hogs by means of a restricted diet, and to cure the animals promptly by means of catharsis, castor oil or magnesium sulphate.

14. Rommel and Vedder, E.: Jour. Agric. Research, 1915, **5**, 489.

15. Hart, E. B., and McCollum, E. V.: Jour. Biol. Chem., 1914, **19**, 373.

16. In chronic mercurial poisoning the following suggestive symptoms occur: anemia, bleeding and spongy gums, loosening of the teeth, a quickened pulse, ulcers of the extremities. At times mercury attacks the nervous system, producing palsy. The resemblance is heightened by the fact that calcium metastases have been found in the muscles in experimental scurvy (Hart) comparable to those characteristic of mercurial poisoning.

17. Von Noorden, C.: Berl. klin. Wchnschr., 1913, **50**, 51.

18. Abderhalden, E., and Lampé, A. E.: Ztschr. f. d. ges. Exper. Med., 1913, **1**, 296.

They were led to attempt a cure by this means as they had noted that the polyneuritic pigeons passed very little stool and that the intestines at necropsy were markedly overfilled. They concluded that, particularly in the pig, toxic products are formed in the intestine. These novel experiments gain additional interest in view of similar results reported by McCollum[19] in connection with the scurvy of guinea-pigs. It may be inquired as to the condition of intestines in infantile scurvy. When we search the necropsy protocols for lesions of the intestinal tract we find that in most cases there are merely occasional hemorrhages and swelling of the follicles and of the neighboring mesenteric glands. In some cases there is inflammation or ulceration of the colon.[20]

If a toxin is to be regarded as the proximate cause of infantile scurvy, the question naturally arises as to the nature of the toxin.[21] Is it exogenous or endogenous? There are some sound reasons for believing that the poison generally is not introduced preformed in the food. In the first place, infantile scurvy frequently develops in babies who are given milk of the very best grade; indeed, in contradistinction to rickets, it is not preeminently a disease of the poor. Furthermore, there is no relation between the concentration of the food mixture and its liability to induce scurvy. If, among a large number of infants receiving pasteurized milk from a common source, some are given milk diluted by one-half, others given it diluted by one-third, and still others whole milk, the last group will not show a preponderating tendency to scurvy, as we should expect were the poison contained in the food. Nor is it at all uncommon to encounter scurvy in an infant which has been fed with a very dilute milk mixture. The other side of this question, however, cannot be entirely dismissed. We should bear in mind that stale pasteurized milk is more apt to produce scurvy than freshly pasteurized, a fact which might be interpreted as in favor of an exogenous toxin. Again, the reports of the scurvy of adults being occasioned by decomposed food, as in Nansen's polar expedition and as

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19. McCollum, E. V.: Jour. Am. Med. Assn., 1917, **68,** 1381.

20. There is one lesion in the intestinal tract to which we would call attention, as it was present in a necropsy performed a few years ago and has been recorded by others—a marked injection of the mucous membrane of the first part of the duodenum. Additional significance would seem to be attached to this lesion in view of the fact that it is noted in some necropsy protocols in cases of beriberi and of pellagra. It may well be that this inflammation is the result of products excreted by the liver and poured into the intestine at this point.

21. There are probably many factors which influence the occurrence of scurvy. Certainly climate plays a rôle. We have frequently found that scorbutic symptoms will disappear when infants are placed out of doors and exposed to the sun and air in the spring months. Scurvy is more prevalent in the winter, as is rickets. No doubt general nutritional diseases act as predisposing factors, among which rickets and syphilis are important.

reported on ships so frequently in the past, cannot be disregarded, and seem open to the interpretation as due, in part at least, to food poisoning. The experiments of Jackson and Harley,[22] who produced scurvy in monkeys by feeding them with tainted tinned meat, would seem to fortify this interpretation. But, as we have said, infantile scurvy develops in the overwhelming majority of cases on food which is not decomposed, so that, although we acknowledge the occasional rôle of exogenous poisons, we believe that the toxin is usually elaborated within the human body. As is well known, toxins are continually being formed in the intestinal canal by bacterial growth. We are protected from the deleterious action partly by the counteraction of neutralizing bacteria. Should this protective force fail, the toxins may gain access to the tissues of the body. This is what happens in infantile scurvy. Whether the toxins differ in kind from those normally present in the intestine, or whether they are always the same, it is impossible to say. The various types of scurvy, as well as of rickets and of beriberi, may be due to differences in this regard.

According to this view, infantile scurvy is essentially a scorbutic auto-intoxication or intestinal intoxication; the diet is faulty in not being capable of inhibiting the elaboration of the poison. This raises the question, which must be left open for discussion, as to whether, from an etiologic point of view, infantile scurvy should be regarded as an entity, or whether its symptoms cannot be produced by various poisons, some exogenous and others endogenous, formed as the result of an unbalanced flora in the intestinal canal.

If we consider scurvy an intestinal intoxication, we naturally inquire as to the functioning of the bowels in this disorder. This has been frequently discussed by writers on this subject, but a consensus of opinion is not apparent. Of the cases reported by the American Pediatric Society the bowels were regular in seventy-four instances, irregular in fifteen, constipated in 126, and diarrheal in seventy-seven. This question has assumed additional interest in view of recent experimental work on animals. As has been stated, Abderhalden and Lampé,[18] as well as McCollum,[19] found marked constipation in the course of their experiments. The latter expressed his conclusions in these words: "Scurvy in guinea-pigs is the result of retention of feces. I do not know whether or not the same is true of human scurvy."

Of course, there can be no question as to whether retention of feces by itself can bring about scurvy in infants; this is excluded by the marked instances of constipation frequently encountered among thriving babies. The majority of bottle fed babies and a large number

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22. Jackson, F. G., and Harley, V.: Lancet, London, 1900, p. 1184.

of the breast fed suffer from a greater or less degree of constipation. On looking up our records of infantile scurvy from this point of view, and comparing them with nonscorbutic infants, we have not been able to note a characteristic distinction. Some of the infants which developed scurvy had normal stools as far as gross examination disclosed, others suffered from constipation, while a greater number showed a record of occasional loose stools. In reviewing the cases reported by others it would seem that, as in the report of the American Pediatric Society, this same lack of uniformity is manifest, but that in the advanced cases the stools are more often diarrheal. In this connection we must bear in mind that the malt soup preparation, the diet which, in our experience, has been associated with scurvy most frequently, is essentially laxative and almost never induces constipation. And, on the other hand, the most potent antiscorbutic both for adults and for infants, one which is effective at times when fruit juices have proved unavailing, is potato, a food which has no distinct laxative properties. It may be added, as noted elsewhere, that scurvy was found to develop in infants in spite of their receiving cod liver oil or olive oil for long periods. We do not wish to conclude that the retention of feces is a negligible factor in the scurvy of infants, but rather that its rôle is quite secondary. When we assume that a poison is contained in the intestinal canal, it is evident that catharsis will be of value, and that constipation will aid in its absorption. This is true of all poisoning which occurs by way of the alimentary canal; for example, in lead poisoning, where catharsis has always been granted a distinct therapeutic place. It is probable that marked constipation may be assigned as one of the causes for the frequent occurrence of scurvy and allied intestinal intoxications among the insane, who neglect their bodily functions.

We have said that the value of potato cannot be ascribed to laxative properties. The same is true of orange juice, which is very mildly laxative, and cannot be depended on to relieve constipation in infants. Its therapeutic value in scurvy is probably due to its influence on the flora of the intestine and to its diuretic effect.

It is surprising that attention has not been called to the fact that *there is a diminished excretion of urine in infantile scurvy.* We have frequently observed this phenomenon, and its occurrence has been noted by the nurses. This oliguria is interesting from several points of view. It accounts in part for the edema which is so frequently met with in this disorder, and is of especial interest in connection with the relation of body weight to infantile scurvy. Before noting this disturbance of metabolism we were at a loss to interpret the paradoxical phenomena of a scorbutic infant which was given orange juice

being greatly improved and consuming considerable more food, but nevertheless failing to gain, or even reacting with a loss of weight. It was only when it was noted that the orange juice brought about a sudden outpouring of urine that the explanation was evident. Whereas before orange juice was given a baby urinated but three or four times a day, passing but 4 to 6 ounces of urine, thereafter it urinated fifteen to twenty times a day and passed 20 to 30 ounces of urine. A chart illustrating this condition is appended. It is probable that the citric acid of the orange juice induces the diuretic action. We had at various times tested the curative value of citric acid, considered by Netter[23] to be the essential deficiency of infantile scurvy, but, although we were able to bring about diuresis and to alleviate the symptoms temporarily, we were never able to effect a complete or permanent cure. In this connection we wish to call attention to the fact, mentioned also by Abderhalden and Lampé, that Funk's vitamins are claimed to belong to the pyridin and pyramidin groups, which possess diuretic properties. It is probable that the kidneys play a considerable rôle in infantile scurvy, its clinical course depending to some extent on the activity of their function, and that toxins are eliminated at an early stage by this route. This statement seems warranted in view of the frequency of urinary symptoms in scurvy — casts and blood cells in the urine, and the signs of parenchymatous inflammation which the kidneys may show at necropsy.[24]

Renewed interest has been awakened in the study of scurvy since it has become possible to reproduce the disease in animals. The first experimental work of this kind is generally associated with the names of Holst[25] and his co-workers, who induced scurvy in guinea-pigs by means of a diet of cereal grains. It should be noted, however, that the same result had been accomplished some years previously in this country by Theobald Smith.[26] During the past few years Baumann and Howard[27] have carried out the first metabolism investigations on scorbutic guinea-pigs. Although this work on animals has increased our knowledge considerably and is certain to open new paths of investigation, caution should be exercised in transferring the results to human beings. The fact that we are able to produce scurvy in guinea-

23. Netter, M.: Bull. Soc. pédiat., Paris, 1902, **4**, 298.

24. Pinner, F.: Deutsch. med. Wchnschr., 1896, **22**, 546.

25. Holst, H., and Froelich, D.: Ztschr. f. Hyg. u. Infektionskr., 1912, **72**.

26. In a bulletin on "Bacilli in Swine Disease," published by the Bureau of Animal Industry, 1895-1896, Theobald Smith says (p. 172): "When guinea-pigs are fed with cereals (it has been observed for some years in this laboratory), with bran and oats mixed, without any grass, clover or succulent vegetables, such as cabbage, a peculiar disease, chiefly recognizable by subcutaneous extravasation of blood, carries them off in from four to eight weeks."

27. Baumann, L., and Howard, C. P.: Am. Jour. Med. Sc., 1917, **153**, 650.

pigs by means of raw milk, a diet which effects a cure in infants, is evidence that some of the underlying conditions are different. An elaborate investigation on guinea-pig scurvy has recently appeared comprising papers by Jackson and Moody[28] and Jackson and Moore,[29] one entitled "Studies on Experimental Scurvy in Guinea-Pigs," the other "Bacteriologic Studies on Experimental Scurvy in Guinea-Pigs." The latter article is of especial interest, as it suggest tentatively that scurvy may be a bacterial infection. These investigators cultivated a diplococcus from the tissues of scorbutic animals after death, reproduced hemorrhages by inoculating cultures of these micro-organisms into the circulation, and recovered the bacteria from the tissues some weeks later. This conception of scurvy as an infectious disease has been brought forward from time to time, especially in relation to epidemics of adult scurvy. Some years ago Ausset[30] claimed to have isolated "a pasteurella type of organism" from a case of infantile scurvy, and suggested that it was the causative agent of this disease. On the other hand, Hart,[31] Rehn,[32] Hirschsprung,[33] von Starck,[34] and Schmorl[35] have failed to find bacteria in the blood, although the total number of cultures seems to have been small. Czerny[36] reports negative growth from fluid aspirated from affected joints. Jackson and Moody's results, while most interesting, are open to the criticism that bacteria were found only after death, and that all blood cultures proved negative. This is, as stated, the same experience as has been encountered in infants.

One of the most striking clinical phenomena of infantile scurvy is the marked susceptibility to infection which it entails — the frequent attacks of "grippe," the widespread occurrence of nasal diphtheria, the furunculosis of the skin, the danger of pneumonia in advanced cases. Whether this is to be in part attributed to the disturbance in water metabolism, in view of the fact that a similar susceptibility exists in *Mehlnärschaden* cases, where the tissues likewise contain an excess of water, there is no basis for judging, but the clinical fact is striking and significant.

It is as one of these secondary infections, we believe, that the findings in the guinea-pigs are to be interpreted. In this connection it is

28. Jackson, L., and Moody, A. M.: Jour. Infect. Dis., 1916, **19,** 478.
29. Jackson, L., and Moore, J. J.: Jour. Infect. Dis., 1916, **19,** 511.
30. Ausset, E.: Bull. Soc. pédiat., Paris, 1902, **4.**
31. Hart, C.: Jahrb. f. Kinderh., 1912, **76,** 506.
32. Rehn: Med. Klin., 1907, No. 30, p. 892.
33. Hirschsprung, H.: Jahrb. f. Kinderh., 1896, **41,** 1.
34. von Starck, W.: Handbuch d. Kinderh., Pfaundler and Schlossmann, 1906.
35. Schmorl: Jahrb. f. Kinderh., 1907, **65.**
36. Czerny, A., and Keller, A.: Des Kindes Ernährung, Ernährungstörungen, Leipzig, 1907, **2,** Ch. 6.

well once more to emphasize that when we refer to scurvy we do not regard it as a disease characterized by hemorrhages, but as a nutritional disorder which exists for months before the subperiosteal or other hemorrhages develop. This nutritional disorder, this simple scurvy, is not attributable to a bacterial invasion, although it leads to and is responsible for its occurrence. From the same point of view orange juice and other antiscorbutics are to be considered as of prime value in combating the toxic nutritional disturbance, but of no direct value in doing away with those hemorrhages which are brought about by bacterial infection. A hemorrhage of infectious origin, in contradistinction to those of toxic origin, must be regarded simply as a focal complication. The clinical course of many of these effusions, receding spontaneously or developing as the scorbutic condition improves, shows that they have local and not general significance. It is highly important that blood cultures should be carried out in the course of scurvy, and that particular attention should be paid to the stage of the disorder in which they are made.

Scurvy sometimes occurs in epidemic form. A few years ago we had the opportunity of observing an epidemic of infantile scurvy in connection with an outbreak of "grippe" at the infant asylum. We do not suggest this as a distinct type of this disease, for, as we have just said, infection is common as a secondary stage of scurvy. At times, however, when infection is widespread and scorbutic malnutrition exists among a group of infants, a considerable number of them may become infected and develop a hemorrhagic form of scurvy. It is an outbreak of this kind which we wish to describe in detail.

In February twelve infants in one ward developed fever and soon showed symptoms of various infections: otitis, pneumonia, nephritis, adenitis, etc. Three died of pneumonia; of the nine who recovered, seven suffered from what we shall term infectious scurvy, meaning by this a type of the disorder brought about by superimposing a secondary infection on the primary nutritional disturbance. Some of the infants showed signs of alimentary intoxication; most of them had no fever at the time the hemorrhages occurred, although they may have had a rise of temperature when the infection began. In April a second epidemic of "grippe" took place and three more infants developed scurvy. The signs were mainly hemorrhagic, developing at sites both atypical and typical for scurvy. They occurred as follows: Case 1, left diaphysis of humerus and tibia; face; anterior abdominal wall at site of serum injection; right eyelid; Case 2, abdominal wall; cranium; vertebral column; external ear; Case 3, diaphysis of left femur; Case 4, cranial bones and external ear; Case 5, external ear and face; Case 6, diaphysis of tibia; Case 7, abdomen (Table 2).

These infants were receiving formulas made from milk pasteurized at 160 F. for twenty minutes.

It is striking that many of the hemorrhagic signs above outlined are quite different from those encountered in infantile scurvy. We have never met with such widespread subcutaneous hemorrhages, and have noted them in the literature only in the most advanced cases. But what makes these cases stand out sharply from ordinary scurvy is not

TABLE 2.—DATA OF EPIDEMIC OF SCURVY

Case	Age, Mos.	Weight		Site of Hemorrhages	Date	Diet	Remarks
		Lbs.	Oz.				
1 J. H.	6½	9	6	Humerus, tibia, face	Apr. 19	Breast milk (1 week); breast milk, buttermilk and orange juice	Grippe since end of February; nephritis; v. Pirquet negative
		10	4	Upper eyelid.......	May 9		
2. L. S.	5	12	14	External ear, parietal bones, vertebral column, abdominal wall	May 4	Pasteurized milk formula; orange juice 1 oz. daily since April 22	Twitchings and convulsions; signs of intoxication; red blood cells in urine; fever to 101 F.; v. Pirquet negative
3. A. R.	10	12	8	Femur............	Apr. 19	Pasteurized milk formula; vegetables for a month; orange juice longer; getting orange juice and vegetables	Grippe end of January; again in April; fever until April 17; v. Pirquet positive; gums negative
				Femur again swollen and tender	June 4		
4. D. E.	5	7		Both ears; parietal bones	Apr. 29	Breast milk since April 19; May 30, changed to pasteurized milk	Grippe throughout March; intoxication; nephritis; no relapse although no orange juice given
5. T. K.	10	15	13	Ear and face......	Apr. 27	Pasteurized milk, cereal, vegetable, soup; orange juice since April 15	Two teeth; gums negative; v. Pirquet negative
6, P. G.	4	8	4	Tibia.............	May 8	Pasteurized milk formula	Grippe end of February and first half of March; gained 20 oz. during last month; v. Pirquet negative
7. I. P.	2	6	4	Abdomen..........	Mar. 7	Breast milk for past week	Grippe; probable source of epidemic

so much their exceptional symptomatology as their lack of response to specific therapy. Two had received breast milk for two weeks previous to the onset of symptoms; one an ounce of orange juice for two weeks; one an ounce of orange juice and also vegetable for two months previously; one vegetable and orange for a week; and another vegetable for an indefinite period before the onset. One baby, 9 months old, which had a tender swelling of the diaphysis of the femur in April, had a relapse of symptoms in June in spite of having received

orange juice and vegetables throughout the intervening period. It should be noted that of the seven infants four were under 6 months of age, which, from a practical standpoint, and although subject to exceptions, is rightly regarded as the minimum age for the hemorrhagic stage of this disorder. Again, although two babies had teeth, neither showed spongy gums nor peridental hemorrhage. The swellings of the long bones, however, were quite typical of the subperiosteal hemorrhages of infantile scurvy, and are open to no other clinical diagnosis.

How are we to interpret this picture? The ages of the infants, the distribution of the hemorrhages, the development of signs in some cases in spite of antiscorbutic diet, the sharply defined epidemic character of the disease, distinguish it from the scurvy we commonly meet with. We believe that the epidemic was brought about by a bacterial invasion. Whereas usually scorbutic intoxication must be prolonged for a period of about six months to allow the secondary invasion of bacteria, in this instance, due probably to the peculiar nature of the bacteria, invasion occurred early and in some infants which were receiving an antiscorbutic diet. In most of these instances, however, it should be noted that the infants had been receiving pasteurized milk for months, and the antiscorbutic foodstuff had been added but a few weeks previously. Latent scurvy was prematurely changed to florid scurvy by the presence of a ward infection; an epidemic of "grippe" precipitated an epidemic of scurvy exceptional in its hemorrhagic tendency.

In closing we may add that this epidemic resembles the epidemics of melena neonatorum which occur from time to time in lying-in hospitals and which formerly visited these institutions so frequently. Not long ago we had the opportunity of observing an epidemic of this character where, within a few weeks, some eighteen new-born infants developed hemorrhages at various sites — the umbilical cord, mouth, nose, skin, etc. These cases must also be considered bacterial in nature. Finally, we wish to suggest that many of the reported instances of scurvy in breast fed babies are to be regarded as cases of sepsis grafted on general malnutrition due to syphilis, tuberculosis and undernourishment, rather than as true scurvy.

CONCLUSIONS

One of the several factors in the pathogenesis of infantile scurvy is faulty diet. Pasteurized milk was found to be a contributing cause if it was not fresh — if given twenty-four to forty-eight hours after pasteurization. From this point of view milk pasteurized in the city is preferable to milk pasteurized at the creamery, which reaches the consumer much longer after the heating process. Aging seemed to

play a greater rôle in the production of scurvy than heating, whether the milk was pasteurized or raised to the boiling point. It was found that even raw milk on aging loses its antiscorbutic properties.

Infantile scurvy is not, however, a simple dietary disease. The diet is at fault in allowing the intestinal bacteria to elaborate toxins. It is doubtful whether the toxin is always the same, and therefore whether, from a strictly etiologic standpoint, this disorder should be regarded as an entity. Infantile scurvy is an intestinal intoxication or an autointoxication due to the overgrowth of harmful bacteria in the intestine. It is the product of an unbalanced flora which is no longer controlled by a proper dietary.

Oliguria is a common symptom of scurvy. The mild therapeutic effect of citric acid may be ascribed partly to its diuretic properties. Orange juice also was found to bring about marked diuresis.

One of the striking and important symptoms of scurvy is a susceptibility to infection (furunculosis, nasal diphtheria, "grippe," etc.). Some hemorrhages are due to this secondary infection, and are to be regarded not as scorbutic, but rather as focal complications. Other hemorrhages are truly scorbutic. Scurvy, however, is essentially a disorder characterized by malnutrition and not by hemorrhage, taking months to develop, and, from a clinical point of view, frequently latent or subacute.

Infantile scurvy occurring in epidemic form is described. This results when latent scurvy exists among a number of infants and an infectious disease (such as "grippe") is superadded.

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SOME OBSERVATIONS ON INTESTINAL BACTERIA IN CHILDREN *

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During the past few years there has been a great revival of interest in the bacteriology of the digestive tract. The investigations of Moro,[1] Tissier[2] and others, especially Herter and Kendall[3] in this country, have explained the discrepancy noted since the days of Escherich, that the number of bacteria in the dejecta is much greater than the number of colonies which develop on our plates. They have demonstrated that the gram-positive organisms found in smears of the intestinal contents are equally important with the gram-negative, that they can be freed from the ordinary intestinal bacteria by cultivation in acid broth, and that they are just as much obligate inhabitants of the alimentary canal as are *Bacillus coli communis* and *Bacterium lactis aerogenes*. The old theory that *Bacillus coli* is gram-positive in the intestines and gram-negative in our cultures was thus proved to be untenable, as was usually suspected. Along with this development of our knowledge, Metschnikoff[4] and his followers have attempted to bring about a change in the character of the bacteria in the digestive tract by the administration of food materials containing bacteria producing large quantities of acid from lactose. It was claimed that the ingested bacteria, particularly the so-called Bulgarian bacilli, would overcome and displace the species previously multiplying in the intestine, *Bacillus coli* and the putrefactive anaerobes. Despite the somewhat extravagant claims of this school of investigators, it has not yet been clearly shown that the ingested organisms are definitely implanted on the intestinal mucosa in man, although Rettger's experiments indicate that such a transplantation may occur in small animals.[5] Furthermore, it should also be indicated that the poisonous action of the putrefactive bacteria in the intestine, while possibly evident clinically in selected cases, has not yet

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* From the Bacteriological Laboratory and the Harriet Lane Home, Johns Hopkins University.

1. Moro: Wien. klin. Wchnschr., 1900, **13,** 114.
2. Tissier: Recherches sur la flore intestinale, normale et pathologique du nourrison, 1900.
3. Herter and Kendall: Jour. Biol. Chem., 1910, **1,** 203. Kendall: Ibid., 1909, **6,** 268.
4. Metschnikoff: The Prolongation of Life, Bacteriotherapie.
5. Hull and Rettger: Jour. Bacteriology, 1917, **2,** 47.

been clearly shown experimentally. Finally, there is a good deal of evidence to show that the changes which do occur after the administration of food materials containing Bulgarian bacteria may be due to the chemical constituents of the food, the lactose and the lactic acid, and not due to the bacteria themselves. Nevertheless, the idea that profound changes may occur in the bacteria of the intestinal canal as the cause of pathologic conditions, or as their accompaniment, and that these changes, particularly the development of a gram-positive in place of a gram-negative flora, may be of diagnostic significance and point the way to remedial treatment, has become firmly intrenched in the minds of clinicians. This is not without reason in view of the facts which have been brought out recently. There are, however, many contradictions in the published results, and it may be doubted whether our knowledge of the conditions which must exist in such a large and varied area for bacterial development as the gastric and intestinal mucosa is yet sufficiently accurate to permit any exhaustive generalization which may be applied clinically. In view of these considerations it has seemed to us worth while to take up certain phases of the problem again, and in the present investigation we have limited ourselves to one particular inquiry, namely, to what extent differences in the bacterial flora of children can be correlated with the type of food forming the sole or the chief ingredient of the diet. For the solution of this problem we have been allowed to utilize the dejecta of the breast-fed infants in the maternity ward of the Johns Hopkins Hospital and those of the young children in the Harriet Lane Home.

In the early part of our studies we made routine examinations of about fifty children fed on mother's milk, by the use of the ordinary mediums, such as plain and dextrose agar and dextrose broth in the fermentation tube. As might have been expected, we obtained in these cultures practically nothing but gram-negative bacteria and no information of value was elicited. It was then decided to make an intensive study of a few cases by a careful microscopic examination of the dejecta and by the adoption of special methods for the cultivation of the various kinds of the micro-organisms seen in the smears. It is the results of the examination which now we wish to report.

Smears from the evacuations of children when stained by gentian violet, methylene blue and by Gram's method reveal six different types of organisms as follows:

1. Small gram-negative bacilli.
2. Small gram-positive bacilli.
3. Gram-positive micrococci and streptococci.
4. Gram-positive yeast cells.
5. Large gram-positive bacilli.
6. Spores of various sizes and shapes.

All these various types of organisms can be cultivated by appropriate methods. With ordinary plates, especially if sugar be present in the medium, the gram-negative bacilli tend to overgrow and crowd out the other species, and one finds *Bacillus coli, Bacterium lactis aerogenes, Bacillus alkaligenes* and occasionally some of the rarer liquefiers of the intestines. The small gram-positive bacilli are chiefly aciduric organisms. They do not appear on agar plates, but may be cultivated on acid broth (2 to 3 per cent.) which inhibits the other species. After two or three transfers in this medium, which suffices usually to effect a separation, these aciduric organisms can be obtained in pure culture on agar or blood serum. They grow well on acid agar and in our experience grow best on acid whey agar. This group evidently represents the aciduric organisms of Moro, *Bacillus acidophilus,* although at times we have encountered species which resemble those described by Heinemann and which he puts provisionally in the group of Bulgarian bacilli. The yeast cells seldom appear on plain agar plates. They grow out abundantly in acid broth with the aciduric bacilli, but can also be obtained on acid whey agar plates. They grow best on dextrose agar plates made directly from the dejecta, where they appear after the lapse of six to ten days, when the agar has become highly acid from the growth of *Bacillus coli.* In such old plates the large viscid colonies of the yeast cells are easily recognized. The greatest interest attaches to the larger gram-positive bacilli of the intestines. They are of various sizes, sometimes small, measuring 0.5 to 0.75 by 2 to 3 microns, sometimes large, measuring 1 to 1.5 by 3 to 8 microns. Their protoplasm may be regular as in the smaller forms, or highly irregular as in the large forms, which seem to be made up of spherical bodies. These organisms appear occasionally on agar plates. They can best be cultivated by heating portions of the dejecta in broth to 85 C. for ten minutes, pouring plates at once, and after twenty-four hours' incubation of this broth. By such a procedure an abundant growth of organisms can be obtained which can now be identified as the aerobic spore-bearing bacteria found in soil, dust, water and milk. In plates poured directly these species have the same morphology as that observed in the smears, and it is sometimes possible, on bacterioscopic examination, to give a provisional opinion as to the species which can be cultivated. This is true especially when the large granular bacilli of the megatherium-petasites group are found. The species cultivated from heated material, immediately and after incubation, are much more varied. The size and shape of the spores produced by these organisms are quite characteristic and can usually be correlated with the spores found in the smears.

We have examined the spore-bearing bacteria on plates of the dejecta in about fifty cases, and we are of the opinion that they repre-

sent the large gram-positive bacteria and the spores found in smears. We see no reason to believe that these gram-positive organisms are anaerobes. The resemblance in morphology of the aerobic spore-bearers cultivated, both in the vegetative state and in the spore state, to the vegetative rods and the spores found in smears is so marked as to lead to the opinion that they are the same. We do not deny the possibility that anaerobic bacteria are present in the intestinal tract in probably all cases. We believe, however, that the majority of the gram-positive rods and the spores represent aerobic species. Of special interest is the occasional presence of a small organism with a round terminal spore looking not unlike the tetanus bacillus. The finding of this organism is sometimes regarded as indicative of intestinal putrefaction, since it has been identified on the basis of its morphology alone as *Bacillus putrificus coli* of Bienstock. This organism can be cultivated without difficulty and can now be recognized as one of the common aerobic spore-bearers, *Bacillus pseudotetanus.*

We have been able to examine somewhat exhaustively the dejecta of ten breast fed babies and of eighteen artificially fed children, varying in age from 1 to 10 years. These latter were fed on a mixed diet, on raw and boiled cow's milk, on buttermilk or on protein milk. The gram-negative bacilli have shown no variation in the different cases. Except in rare instances, they are the most abundant of the species present and they can always be cultivated on agar plates. The aciduric bacilli were obtained in seven of the ten breast fed babies and in all of the eighteen children. There was no particular predominance of these organisms except in one case, and their presence although in small numbers in all of the artificially fed children and in 70 per cent. of the breast fed infants suggests that they could always be found were the search extended. In one instance the stool of a normal suckling was made up almost exclusively of long gram-positive bacilli which could not be cultivated by any method tried. Branching aciduric organisms of the type of *Bacillus bifidus* were not encountered in our series either in the breast fed or in the artificially fed children. Gram-positive micrococci and streptococci were found in six of the ten babies and in ten of the eighteen artificially fed children. Many of these were distinctly aciduric; others, however, were streptococci which grow on ordinary plates, while others were evidently *Micrococcus ovalis.* As far as could be learned, no significance is to be attached to the presence of organisms of this group, but the fact that they were isolated from 60 per cent. of cases leads to the opinion that like the aciduric bacilli they are obligate inhabitants of the intestinal canal. Yeasts were obtained in six of the eighteen children. In two of these cases the children were fed on buttermilk, which on culture proved to contain yeasts in great numbers. In three other cases milk was the chief

article of diet and in one instance the child was being nourished on protein milk. In one case the stool of a six weeks' baby suffering from pyloric stenosis and fed on breast milk was also full of yeasts.

In the dejecta of the breast fed children aerobic spore-bearing bacteria were obtained in all but one case. They were present in considerable variety in the original smears, even in the youngest nurslings, evidently finding their way into the alimentary canal of the child as soon as it begins to swallow. They were not so abundant as to grow out on plates made directly from the dejecta or to any extent from heated material before its incubation. They could, however, always be obtained from this material after incubation for twenty-four hours. In two cases the spore-bearing bacteria were markedly increased in these breast fed children. They appeared in great profusion on our original plates and in plates poured directly from heated material. In one of these cases the stool was made up largely of meconium mixed with a soap suppository and in the other case the stool was very scanty and material for cultures had to be scraped from the napkin. We do not, therefore, regard these cases as indicative of any real increase of spore-bearers in the intestinal tract. The spore-bearers found in breast fed children were chiefly those species which have now been shown to be the prevalent bacteria of our environment. *Bacillus cereus* and *Bacillus albolactus* were the most frequent isolations, *Bacillus pseudotetanus* and *Bacillus mesentericus* were somewhat less common, while *Bacillus subtilis, Bacillus petasites* and *Bacillus vulgatus* were among the rarer findings. This relative proportion of the species is about the same as the proportion established for soil, dust and water in Baltimore in which *Bacillus cereus* and *Bacillus albolactus* are the most abundant.[6] It is interesting to note that often the same organisms were isolated from different patients on the same day, pointing to some sort of a ward infection as their source.

In the artificially nourished children aerobic spore-bearers were found in smears from the dejecta in all instances. In three cases they were not isolated from plates made from either the raw or heated material. One of these was a child with pyloric stenosis fed on breast milk and formula, another was a child with pneumonia fed on mother's milk and barley water, and the third was a child with ileocolitis fed on protein milk and formula. The aerobic spore-bearers were cultivated in 15 of the 18 cases. Practically the same varieties were found as in the breast fed children, *Bacillus cereus* and *Bacillus albolactus* being the most common. Pseudotetanus bacilli and members of the megaterium and mesentericus groups were also isolated. There was an increase of gram-positive aerobic spore-bearers in ten of the 18 cases.

6. Lawrence and Ford: Jour. Bacteriology, 1916, **1**, 273. Laubach: Jour. Bacteriology, 1916, **1**, 493.

The organisms of this character were greatly increased in numbers in the smears, and cultures showed them in abundance in the heated and incubated material. In 6 of these cases these species were so abundant as to appear in large numbers on the plates poured directly from the dejecta. In 8 of these 10 cases the children were fed on protein milk; in 5 of these the stools were normal, in 1 case constipated, in 1 case semisolid and in 1 case diarrheal. Of the 2 other cases with an increase in spore-bearers, one child was suffering from diarrhea and was being fed on buttermilk; the other was a feeding case with normal stools. From this patient material was examined on four different occasions. No increase in spore-bearers was detected on the first three examinations, at which time the patient was being nourished on whole milk, barley water and sugar. Subsequently, wheat flour and malt soup were added to this diet, and the next examination showed an increase of spore-bearing bacteria. Eight of the artificially fed children failed to show any increase of large gram-positive bacteria. One of these patients was fed on protein milk and one on buttermilk. The others were receiving either a general diet, breast milk mixed with barley water, or cow's milk and barley water. We thus see that, with two exceptions, an increase of aerobic, spore-bearing bacteria in the intestinal discharges, gram-positive in character, is regularly associated with a diet of protein milk or buttermilk.

The question now arises as to the explanation of this association, which we believe to be quite definite. Does the diet of protein milk or buttermilk, for instance, so change the character of the intestinal contents as to lead to profound alterations in the conditions for bacterial development, or is there a possibility that these organisms make their way into the alimentary canal with the food and find there either a temporary or a permanent nidus for development? We believe this latter explanation to be the correct one. To throw some light on this question a bacterologic examination of the various foods employed in the Harriet Lane Home was undertaken, including pasteurized milk, protein milk, buttermilk and farina. All these articles of diet were found to be infected with aerobic, spore-bearing bacteria, the spores of which are capable of withstanding the heat employed in ordinary cooking. The bacteria found in protein milk and in buttermilk were especially abundant, *Bacillus cereus* and *Bacillus albolactus* being the predominant types. In the heated milk they were somewhat less common, the same species predominating. Farina was relatively free from bacteria and in the samples examined contained chiefly pseudotetanus bacilli. The various articles of diet contained the following species of bacteria:

Protein Milk: *Bacillus cereus, Bacillus albolactus, Bacillus mesentericus, Streptococci,* molds.

Heated Milk: *Bacillus cereus, Bacillus albolactus, Bacillus mesentericus,* micrococci, molds.

Buttermilk: *Bacillus cereus, Bacillus albolactus, Bacillus mesentericus,* yeasts, molds.

Farina: *Bacillus pseudotetanus, Bacillus cereus, Bacillus albolactus, Bacillus mesentericus,* molds.

From the results of this examination it may be seen that the bacteria with which the food is infected are almost the same as those found in the dejecta of the children fed on these foods. *Bacillus cereus* and *Bacillus albolactus* are the most common, while *Bacillus mesentericus* and *Bacillus pseudotetanus* also appear. The relative proportion of the species encountered in the food is also strikingly similar to that established for the dejecta. We are, therefore, inclined to the opinion that the presence of aerobic spore-bearing bacteria, gram-positive in character in the dejecta of children, is to be attributed to their mechanical introduction with the richly infected food. This we believe particularly striking in the cases in which the children are fed on protein milk and buttermilk. That a change in the chemical ingredients of the food employed may be the causative factor in the appearance of the large gram-positive bacteria in the dejecta is not ruled out by our methods of investigation and for the present our conclusion cannot be regarded as anything more than a well defined opinion. We hope to clear up this point in future studies. We see no reason to believe that the presence of large gram-positive organisms is indicative of anaerobic putrefaction, however, nor is it of any diagnostic value, since it occurs with a variety of clinical conditions. It is possible that we have here an actual substitution of bacterial species in the intestine, but whether this substitution is temporary or permanent is not clear from the work thus far completed. It is interesting to note that the results of this work lend no support to the old contention of Flügge[7] that the resistant spore-bearing organisms which survive in boiled milk may pass through the acid gastric juice, multiply in the alkaline contents of the lower bowel and by their toxic products set up diarrheal conditions. The presence of normal, constipated or loose stools in cases in which there is a great increase in aerobic spore-bearers indicates that these organisms may be regarded as practically harmless in the alimentary canal, even if they be present there in large numbers. Finally, our results indicate that one should be extremely cautious in drawing any conclusions which have a clinical bearing from a bacteriologic examination of the dejecta unless a study of the bacteria in the ingested food be made at the same time.

7. Flügge: Ztschr. f. Hyg., 1894, **17,** 272.

CASES EXAMINED

BREAST-FED CHILDREN

Case 1.—H., 3 to 4 days; stool normal. Smears showed gram-negative bacilli, gram-positive cocci and a few large gram-positive bacilli. Cultures revealed *Bacillus coli,* aciduric cocci and four spore-bearers in small numbers, *Bacillus cereus, Bacillus pseudotetanus, Bacillus mesentericus* and *Bacillus petasites.* No increase of spore-bearers.

Case 2.—J., 4 days; stool normal. Smears showed gram-negative bacilli, small gram-positive bacilli and cocci and large gram-positive bacilli and oval spores. Cultures revealed *Bacillus coli, Bacillus cereus* and *Bacillus albolactus* in considerable numbers. This stool was small, chiefly meconium, and in making the cultures the material had to be scraped from the napkin. The increase of spore-bearers may be explained on this basis.

Case 3.—P., 7 days; stool normal. Smears showed chiefly gram-negative bacilli, gram-positive cocci and large gram-positive bacilli with some terminal spored organisms. Cultures revealed *Bacillus coli,* aciduric bacilli and *Bacillus cereus* in great numbers. This stool was obtained by means of a soap suppository, and the increase of spore-bearers may have been due to this factor.

Case 4.—P., 15 days; stool normal. Smears showed gram-negative bacilli and a few large gram-positive bacilli. Cultures gave *Bacillus coli* and *Bacillus cereus.* No increase of spore-bearers.

Case 5.—B., 5 days; stool normal. Smears showed gram-negative bacilli, small gram-positive bacilli, large gram-positive bacilli and large cocci. Cultures revealed *Bacillus coli,* aciduric cocci, *Bacillus cereus* and *Bacillus mesentericus.* No increase of spore-bearers.

Case 6.—K., 12 days; stool normal. Smears showed gram-negative bacilli and small gram-positive bacilli. Cultures revealed *Bacillus coli,* aciduric bacilli and cocci, *Bacillus pseudotetanus* and *Bacillus petasites.* No increase of spore-bearers.

Case 7.—G., 5 weeks; stool normal. Smears showed gram-negative bacilli, small gram-positive bacilli and cocci. Cultures showed *Bacillus coli,* aciduric bacilli and cocci, *Bacillus cereus* and *Bacillus pseudotetanus.* No increase in spore-bearers.

Case 8.—W., 19 days; stool normal. Smears showed gram-negative bacilli, gram-positive cocci. Cultures revealed *Bacillus coli,* aciduric bacilli and cocci and *Bacillus pseudotetanus.* No increase of spore-bearers.

Case 9.—M., 8 months; stool normal. Smears showed gram-negative bacilli, small gram-positive bacilli and large gram-positive bacilli. Cultures revealed *Bacillus coli,* aciduric bacilli and cocci and a variety of spore-bearers in small numbers, *Bacillus cereus, Bacillus pseudotetanus, Bacillus vulgaris* and *Bacillus mesentericus.* No increase of spore-bearers.

Case 10.—R., 6 weeks (Harriet Lane Home). Pyloric stenosis; stool normal; breast fed. Smears showed very few gram-positive bacilli, many thin, rather long gram-positive bacilli, a typical gram-positive flora. No large gram-positive organisms were found. Cultures revealed aciduric cocci and aciduric bacilli of a different morphology from that of the organisms seen in the smear. Yeast cultivated. No spore-bearers found.

ARTIFICIALLY FED CHILDREN

Case 11.—N. S., 3 months (H. L. H.). Feeding case; stool normal. Diet, whole milk, barley water and cane sugar. Stools examined on four occasions. Smears showed small gram-negative bacilli, small gram-positive bacilli and micrococci, large gram-positive bacilli and terminal spored organisms. Cultures showed *Bacillus coli,* aciduric bacilli and micrococci and yeasts, together with

Bacillus cereus, Bacillus albolactus and *Bacillus pseudotetanus.* No increase of spore-bearers. In this case there was a good deal of variation in the amount of sugar in the diet, and wheat flour and malt soup were added to the whole milk and barley water, after which the spore-bearers were definitely increased.

Case 12.—B., 6 weeks (H. L. H.). Diarrhea; stools numerous and watery. Diet, breast milk and buttermilk. Smears from the stool showed gram-negative bacilli, small gram-positive bacilli and large gram-positive bacilli. Cultures showed *Bacillus coli,* aciduric bacilli, and *Bacillus cereus.* Spore-bearers increased.

Case 13.—K., 4 years (H. L. H.). Intestinal indigestion; stool large, semisolid, foul, pasty and full of fat and undigested meat fibers. Diet, protein milk and junket. Two examinations. Smears showed gram-negative bacilli, small gram-positive bacilli, large gram-positive cocci, large gram-positive bacilli. Cultures showed *Bacillus coli,* aciduric bacilli and micrococci, and *Bacillus cereus.* No increase of spore-bearers in the first examination on admission to the hospital. On second examination, after a diet of protein milk and junket was established, the spore-bearers were definitely increased.

Case 14.—P., 3 months (H. L. H.). Fatal diarrhea; stools numerous, watery, containing a small amount of mucus and numerous curds, varying in size from that of a small pea to that of a small lima bean. The vomitus contained the same curds. Diet, protein milk and buttermilk. Stools examined three times. Smears showed gram-negative bacilli, small gram-positive bacilli and cocci, large gram-positive bacilli. Cultures revealed *Bacillus coli,* aciduric bacilli and micrococci, and yeasts, together with *Bacillus cereus, Bacillus albolactus* and *Bacillus mesentericus.* Spore-bearers increased. The curds showed a few gram-negative bacilli, many gram-positive cocci and yeasts and a great predominance of gram-positive bacilli. Cultures from them revealed yeasts and the three species mentioned above in overwhelming numbers. Their presence in the vegetative state in the curds is suggestive of an actual multiplication in the passage of the curds through the alimentary canal.

Case 15.—H., 2 years (H. L. H.). Acidosis; stools frequent, foul, watery and bloody. Diet, buttermilk and farina. Two examinations. Smears showed gram-negative bacilli, small gram-positive bacilli and micrococci, large gram-positive bacilli, yeasts and spores. Cultures revealed *Bacillus coli,* aciduric bacilli, yeasts, *Bacillus cereus, Bacillus albolactus* and *Bacillus mesentericus.* No increase of spore-bearers.

Case 16.—D. (H. L. H.). Fatal acidosis; stools numerous and watery. Diet general and restricted. Smears showed gram-negative bacilli, small gram-positive bacilli and cocci, large gram-positive bacilli, yeasts, oval spores and terminal-spored bacilli. Cultures revealed *Bacillus coli,* aciduric bacilli, together with *Bacillus cereus, Bacillus subtilis* and *Bacillus albolactus.* No increase of spore-bearers.

Case 17.—W., 1 year (H. L. H.). Pneumonia; stools large and constipated. Diet, heated milk, barley water, farina and orange juice. Smears showed gram-negative bacilli, small gram-positive bacilli and cocci, large gram-positive bacilli, spores and yeasts. Cultures revealed *Bacillus coli, Bacillus lactis aerogenes,* aciduric bacilli and cocci, yeasts and *Bacillus cereus.* No increase of spore-bearers.

Case 18.—W., 7 months (H. L. H.). Pneumonia; stools frequent, watery. Diet, protein milk. Smears showed gram-negative bacilli, gram-positive cocci, large gram-positive bacilli. Cultures revealed *Bacillus coli, Bacillus lactis aerogenes,* aciduric bacilli and cocci, together with *Bacillus cereus.* No increase of spore-bearers.

Case 19.—B. W., 5 months (H. L. H.). Eczema; stool normal. Diet, milk, barley water, sugar and farina. Smears showed gram-negative bacilli, small gram-positive bacilli and cocci and large gram-positive bacilli. Cultures revealed

Bacillus coli, aciduric bacilli and cocci, yeasts, together with *Bacillus cereus* and *Bacillus pseudotetanus.* No increase of spore-bearers.

CASE 20.—L., 8 months (H. L. H.). Feeding case after diarrhea; stools normal. Diet, protein milk and buttermilk. Smears showed gram-negative bacilli, small gram-positive bacilli and large gram-positive bacilli. Cultures revealed *Bacillus coli,* aciduric bacilli and cocci, together with *Bacillus cereus, Bacillus albolactus* and *Bacillus pseudotetanus.* Spore-bearers increased.

CASE 21.—H., 3 months (H. L. H.). Diet, protein milk. Smears showed gram-negative bacilli, small gram-positive bacilli and cocci, large gram-positive bacilli. Cultures revealed *Bacillus coli,* aciduric bacilli, yeasts and several of the common spore-bearers. Spore-bearers increased.

CASE 22.—B., 10 months (H. L. H.). Acidosis; stools large and constipated. Diet, protein milk and dextromaltose. Smears showed small and medium sized gram-negative bacilli, gram-positive diplococci or short streptococci, small gram-positive bacilli and large gram-positive bacilli in considerable numbers. These last were of various sizes and shapes. Some had round ends, others square ends and many showed degenerated cytoplasm. A few very large gram-positive organisms were found with large subterminal spores. Small spores of the subtilis or mesentericus type were also found. Cultures revealed *Bacillus coli,* aciduric bacilli, *Micrococcus ovalis* and *Bacillus subtilis.* The plates from the raw material showed no increase of spore-bearers. Plates from the heated material before and after incubation showed many colonies of *Bacillus subtilis.*

CASE 23.—W., 8 months (H. L. H.). Acidosis and polyuria; stools normal. Diet, protein milk and dextromaltose. Smears showed small and medium sized gram-negative bacilli, small gram-positive bacilli, small and large gram-positive diplococci and a great increase of large gram-positive bacilli. These last were of various sizes and shapes, some with round ends, others with square ends resembling *Bacillus cereus* or *Bacillus megaterium* in morphology. Cultures revealed *Bacillus coli, Micrococcus ovalis,* aciduric bacilli and cocci, and *Bacillus subtilis.* No increase of spore-bearers on plates made from raw material. *Bacillus subtilis* in great profusion on plates made from heated material, both before and after incubation.

CASE 24.—A., 7 months (H. L. H.). Pneumonia; stools constipated. Diet, breast milk and barley water. Smears showed small and medium sized gram-negative bacilli and diplococci, small gram-positive bacilli and diplococci. No large gram-positive organisms seen. Cultures revealed *Bacillus coli,* aciduric bacilli and cocci. No spore-bearers isolated from raw material or from heated material before or after incubation.

CASE 25.—Q., 7 to 8 months (H. L. H.). Ileocolitis; stools loose. Diet, protein milk and formula. Smears showed small and medium sized gram-negative bacilli, gram-positive diplococci, and large gram-positive bacilli. The latter were abundant but not increased. Cultures revealed *Bacillus coli,* aciduric bacilli and micrococci and terminal-spored bacilli growing in acid broth. No spore-bearers cultivated from raw material or from heated material either before or after incubation.

CASE 26.—S., 9 to 12 months (H. L. H.). Furunculosis, with possible diagnosis of scurvy; stools normal. Diet, protein milk, junket and orange juice. Smears showed small and medium sized gram-negative bacilli, small gram-positive bacilli, gram-positive diplococci and large gram-positive bacilli with occasionally degenerated cytoplasm. Large gram-positive bacilli increased in number in the smears. Cultures revealed *Bacillus coli,* aciduric bacilli, and *Bacillus subtilis.* No increase of spore-bearers on plates from raw or heated material.

CASE 27.—C., 19 months (H. L. H.). Anemia and throat infection; stools normal. Diet, protein milk. Smears showed small and medium sized gram-negative bacilli, small gram-positive bacilli and diplococci and large gram-

positive bacilli much increased in number. The latter were in many instances sporulating with spores in the center and degenerated cytoplasm. Cultures revealed *Bacillus coli,* aciduric bacilli, and *Bacillus subtilis.* No increase of spore-bearers on plates from raw or heated material.

CASE 28.—S., 2 months (H. L. H.). Pyloric stenosis; stools normal. Diet, breast milk and formula. Smears showed small gram-negative bacilli, rather small, long and thin gram-positive bacilli, gram-positive diplococci, and a few large gram-positive bacilli with subterminal spores. Cultures revealed aciduric bacilli and cocci and an unknown aciduric spore-bearer. No other spore-bearers isolated from either the raw or heated material.

THE RELATION OF THE REACTION OF THE URINE TO THE DIET IN INFANTS AND CHILDREN *

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In the treatment of diseases of children there are many indications for changing the reaction of the urine. To bring about this change is often a matter of great difficulty. I believe the majority of failures are due to a lack of a proper dietary regulation, without which drugs may prove of no avail, much to the surprise of the physician.

INDICATIONS FOR CHANGING THE REACTION OF THE URINE

1. The principal indication for changing the reaction of the urine in children is pyelitis, the treatments for which are nearly all founded on these changes. The principles of such treatments are:

(*a*). *Render the urine alkaline,* because it is less irritant to the inflamed mucous membranes and helps to dissolve the mucous and pus.

(*b*) The use of hexamethylenamin, which is considered one of the best antiseptics for the urinary tract. But hexamethylenamin acts only by splitting into ammonia and formaldehyd, the formaldehyd having the antiseptic action; this splitting occurs in appreciable amounts only when the urine is acid.

(*c*). The alternation of these two treatments (*a* and *b*); that is, the changing from alkaline to acid and then from acid to alkaline, etc., hexamethylenamin being given or not during the acid periods.

These changes are supposed to make the surroundings unsuitable for the growth of bacteria, and have the advantage of avoiding the continuous irritative action of the formaldehyd on the urinary tract.

2. *Detroying and preventing crystals and calculi.* The most frequent, and perhaps the only crystals found in children's urine are those formed by uric acid or urates.

(*a*). The urate crystals are formed in acid urines, and some of them, particularly sodium urate, are apt to cause hematuria. An alkaline urine might prevent their formation.

(*b*). *Calculi.* Alkalinity cannot dissolve calculi, but it prevents the precipitation of uric acid and urates, which may occur to a serious extent only in acid urines.

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In a few instances it has been observed that alkalinity caused the breaking up of large stones into small fragments. This cannot be attributed to the solution of the uric acid; the explanation probably is that the calculi were composed of small fragments glued together by mucous, and that the alkalies merely caused the solution of the latter.

3. Acid urine is, as already stated, irritating to the mucous membranes and somewhat to the external genitalia, which often is the cause of masturbation in female children. Acid urine may also possibly cause eneuresis. A change to alkalinity will usually relieve the irritation and dissolve any mucus that may be present.

4. An excess of uric acid in the urine may cause abdominal pains which would be very difficult to diagnose without an examination of the urine. Rendering the urine alkaline might prevent the further formation of the uric acid, or at least make it less troublesome.

5. Alkaline urine has a diuretic action, which, with its antiirritative action, has to be considered in the treatment of nephritis.

6. In cases of acidosis the acid in the urine is a consequence of the excess of acids in the blood. The change of the reaction of the urine is an index of the results of treatment and the progress of the disease.

METHOD FOR TESTING THE REACTION OF THE URINE

The real acidity of the urine, that is, the number of hydrogen ions, can be determined by the indicator method, or by the gas chain method, the former being the simpler.

I used the method of titrating the acidity by means of a tenth-normal or hundredth-normal solution of sodium hydrate which is added up to neutralization, phenolphthalein being used as the indicator. This is a very simple method and seems to have been sufficiently accurate as far as the final results are concerned.

If one desires to compute the number of grams of hydrogen in each 100 c.c. of urine it is necessary to multiply by 0.1 the number of cubic centimeters of tenth-normal sodium hydrate solution used in neutralizing the 10 c.c. of urine.

Dry potassium oxalate must be previously added to the urine in order to precipitate the lime salts which otherwise would precipitate the phosphates when the hydrate is added. Six grams should be added for each 10 c.c. of urine used.

When litmus is used, it must be remembered that the urine may be found alkaline, while it may be acid to phenolphthalein.

In testing the degree of alkalinity of a urine, I used a sulphuric acid solution equivalent to the strength of the sodium hydrate, with the same indicator.

HOW TO CHANGE THE REACTION BY DIETARY PROCEDURE

In studying the relation of diet to urinary reaction, I have considered the following phenomena, which, in part, were responsible for this investigation:

1. The urine of the carnivora is acid, and that of the herbivora is alkaline.

2. The acidity of the urine of the carnivora depends especially on the products of protein metabolism. Sulphur occurs in an unoxidized condition. Phosphoric acid occurs in nucleic acid, in neucleoproteins, in pseudonucleins and in lecithin. During metabolism these are oxidized into sulphuric acid or set free as phosphoric acid, thus accounting for the acidity of the urine.

3. There are also organic acids such as phenylacetic, benzoic, uric, urocyanic, etc., which are formed by oxidation of certain protein constituents, and contribute also to the acidity of the urine.

Nitrogen from the proteins is eliminated in the unoxidized form as urea for the most part, but this is a very weak base, practically neutral in reaction, and hence is not capable of neutralizing the acid produced.

4. The alkaline reaction of the urine of the herbivorous animals is due to the fact that vegetables and fruits contain salts. Some of these salts are neutral; others are acid salts of dibasic or polybasic acids or other carboxylic acids, as, for example, acid potassium malate, citrate, acetate, tartrate, etc.

On oxidation in the body these salts are burned to carbonates. Some of them are excreted through the lungs in the form of carbonic acid, leaving the disassociated base — usually sodium or potassium — to reunite with the very weak acid, carbonic acid, and in this form is excreted in the urine. These carbonates have an alkaline reaction owing to their giving rise to free alkali by hydrolysis. This explains why lemonade or orange juice makes the urine alkaline.

The vegetable proteins, on the other hand, are not absorbed as well as the animal proteins, and their products of metabolism are more apt to be found in the stools.

5. In starvation, the acidity of the urine increases, owing to the breaking down and digestion of the tissue proteins, which of course are animal in origin.

6. During the infectious diseases, also, the absorption of protein products is increased, especially those of the nucleic group, giving rise to an especially acid urine.

From all these facts, I arrive at two theoretical conclusions:

1. The more protein in the food (especially of the nucleic type) the more acid the urine.

2. A diet of vegetables, especially of those poor in proteins, diminishes the acidity of the urine.

With these theories as a starting point, the following experiments were undertaken, first on babies, and then on older children. Bottle fed babies rather than breast fed babies were used because of the impracticability of changing the percentage of the elements of the breast milk. This was readily done with the bottle feedings. The three babies used were on formulas of which the exact percentages of fat, carbohydrate and protein were known. These percentages were changed at will during the course of the experiments.

The results are shown in Charts 1, 2 and 3. The circles represent the grams of protein in the diet per kilo of body weight; the solid dots represent the number of cubic centimeters of tenth-normal sodium hydrate or sulphuric acid solution necessary to neutralize 10 c.c. of the whole twenty-four-hour amount of urine.

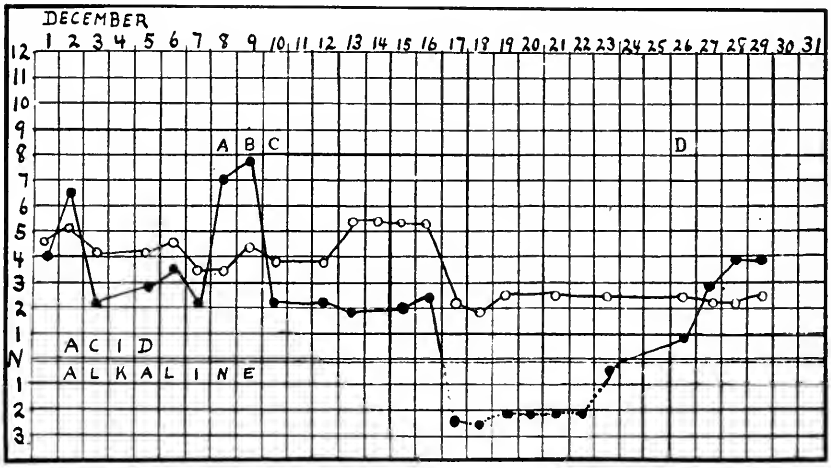

Chart 1.—The relation of feeding and other factors on the reaction of the urine in an infant: *A,* infant lost 100 gm.; *B,* lost 150 gm.; *C,* regained 100 gm.; otitis media.

EXPERIMENTS

Baby 5 months old (Chart 1). Started on a formula containing fat, 2 per cent.; dextrimaltose, 6 per cent.; protein, 2.50 per cent. (880 c.c.). As the baby weighed 4,620 gm., it was getting 4.7 gm. of protein per kilo of body weight. The acidity of the urine on the first day was 4; that is, it took 4 c.c. of tenth-normal sodium hydrate solution to neutralize 10 c.c. of urine. The next few days, although the percentage of protein in the food was not changed, the baby's daily total food intake and weight necessarily varied a little, thus accounting for the irregularity in the curve representing the relation of grams of protein in the food to the kilo of body weight. This variation holds throughout all these experiments.

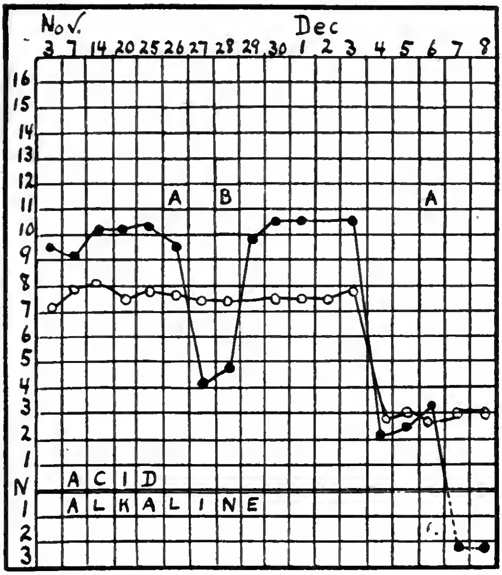

Chart 2.—The relation of feeding and other factors on the reaction of the urine in an infant: *A,* infant fed cereal soup; *B,* cereal soup omitted.

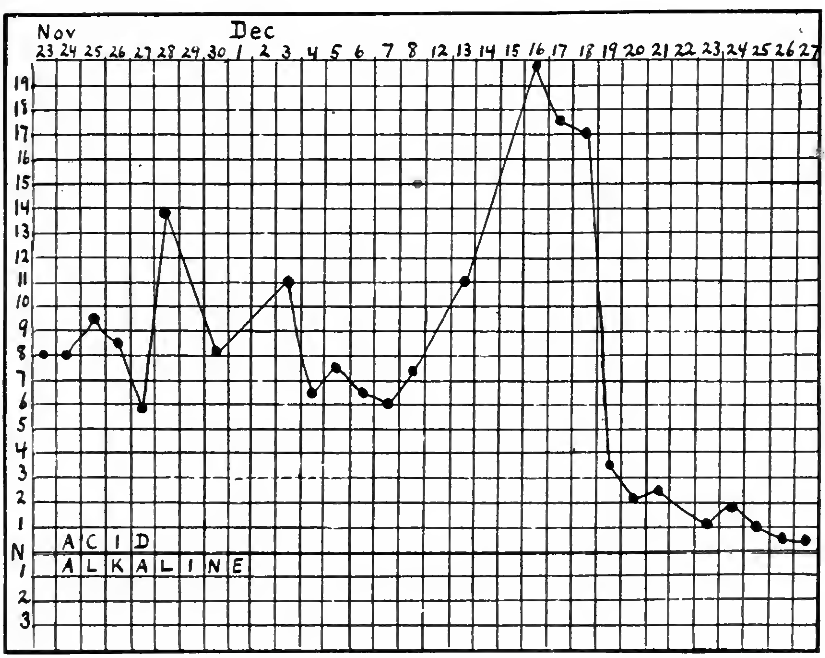

Chart 3.—Irregular acidity of the urine on an unchanged diet.

December 8, the acidity suddenly rose to 7 c.c. with no change in the food. It happened that the baby lost 110 gm. of weight on that day, due to a nasopharyngitis accompanied by a slight fever. December 9, there was a further loss of 150 gm.; the acidity rose again. December 10, the baby was better and gained back 100 gm.; the acidity immediately dropped to the level at which it was before the onset of the fever and remained there.

December 17, the protein in the food was dropped from 2.50 per cent. to 0.90 per cent. This protein represented 1.9 gm. per kilo of body weight on December 18. The urine became alkaline, so that 2.2 c.c. of tenth-normal sulphuric acid was necessary to render 10 c.c. of it neutral.

December 26, an otitis media developed. The acidity of the urine rose immediately. A transfer of the baby to another bed made further experimentation impossible.

Baby 8 months old (Chart 2), weight 5,110 gm., November 3 was given a formula representing fat 2.50 per cent., lactose 5.50 per cent., protein 3.20 per cent. The baby took about 1,170 c.c. of food a day; this afforded 7.3 gm. of protein per kilo of body weight. The acidity of the urine remained at about 9 or 10 c.c. until November 27, when a sharp drop in the acidity was noted. I learned that on the day before, cereal soup had been ordered twice a day. Two days later I asked to have the cereal omitted, and without it the acidity again rose to its former level.

December 3, the protein was diminished from 3.20 per cent. to 2 per cent. This new formula gave about 2.9 gm. of protein per kilo of body weight. The acidity decreased immediately to 2 or 3 c.c., but the urine did not become alkaline. As a matter of interest, the cereal soup was started again December 6, and a marked degree of alkalinity resulted—over 2 c.c.

Baby 8 months of age (Chart 3), was started, November 23, on a formula containing 3 per cent. protein, representing 6.6 gm. of protein per kilo of body weight. It is to be noticed how irregular the acidity was in this urine, although the food was unchanged. The acidity began at 8 c.c. and oscillated widely, rising as high as 20 c.c. I cannot explain this wide variation.

December 18, the protein was reduced from 3 per cent. to 1 per cent., giving about 2 gm. of protein per kilo of body weight. The acidity of the urine dropped immediately to 2 c.c. and remained at about the same level during the remainder of the experiment. The addition of a vegetable soup would in all probability have turned the urine alkaline, but the baby left the hospital before this was tried.

These three charts show well what it was hoped the experiments would prove — the effects on the reaction of the urine of infection, starvation, loss of weight, vegetable and protein diets. It is to be noted that the proteins were never fed below the physiologic needs of the body; that is, 1.5 gm. per kilo of body weight. Emphasis must be placed on the fact that it is possible to change the reaction of the urine in bottle fed babies by a simple change in the formula, but that in the presence of fever or loss of weight, it is more difficult to make it alkaline by these same means.

The second series of experiments was made on two children, 5 and 5½ years old. In their diets, of course, the amount of proteins could not be regulated as accurately as with the babies, but in order to make them as accurate as possible, four types of diet were used: 1, vegetable diet; 2, mixed or "House Diet"; 3, milk diet; 4, animal diet. The accompanying table shows the average food percentage and calories of each diet.

TABLE SHOWING FOOD PERCENTAGE AND CALORIES OF VARIOUS DIETS

I. VEGETABLE DIET *

Breakfast	Amount, Gm. or C.c.	Fats, Gm.	Carbohyd., Gm.	Proteins, Gm.
Cereal (rice)	100	1.50	2.00	8.00
Bread	15	0.50	15.00	3.00
Butter	5	5.00		
Dinner				
Bread	30	1.00	30.00	6.00
Tomato	30	0.07	1.40	0.42
1 potato.............	...	1.00	20.00	1.70
Asparagus	30	0.30	0.80	0.45
Cereal	100	1.50	2.00	8.00
Butter	...	5.00		
Supper				
Toast	15	0.50	15.00	3.00
Peas	40	0.40	1.20	8.00
Orangeade	120	0.25	21.25	1.50
Apple sauce..........	125	1.00	46.50	0.25
Total		18.02	155.15	40.32

Total calories, 1,008.03

* 3 gm. protein per kilo; 80 calories per kilo.

II. MIXED DIET †

Breakfast	Amount, Gm. or C.c.	Fats, Gm.	Carbohyd., Gm.	Proteins, Gm.
Potato	...	1.00	20.00	1.70
Milk	120	4.80	5.40	3.80
Bread	30	0.50	15.00	3.00
Dinner				
Chicken	45	4.50	.....	10.00
Soup	100	....	0.60	3.48
Bread	30	0.50	15.00	3.00
Butter	...	5.00		
Potato	...	1.00	20.00	1.70
Supper				
Milk	200	8.00	9.00	6.40
		1.20	1.60	6.40
		0.50	15.00	3.00
Total		27.00	101.60	42.48

Total calories, 913.05

† 72 calories per kilo; 3.5 gm. protein per kilo.

III. MILK DIET ‡

Milk	1,000	40.00	45.00	32.00

Total calories, 687.8

‡ 2.56 gm. of protein per kilo; 55 calories per kilo.

IV. ANIMAL DIET §

Breakfast	Amount, Gm. or C.c.	Fats, Gm.	Carbohyd., Gm.	Proteins, Gm.
1 egg................	...	5.00	....	7.00
Milk	180	7.20	8.10	5.76
Bread	15	0.25	8.00	1.50
Dinner				
1 egg................	....	5.00	....	7.00
Milk	210	8.45	9.45	6.72
Broth	90	0.50	....	10.00
1 chop...............	60	6.00	....	14.00
Supper				
Milk	180	7.20	8.10	5.46
Bread	15	1.50	10.00	1.50
1 egg................	...	5.00	.....	7.00
Total		46.10	43.65	65.94

Total calories, 880.55

§ 5 gm. protein per kilo; 70 calories per kilo.

The weight of the two children was about the same (12,400 and 12,550 gm.); therefore, they were getting about the same number of calories and the same amount of protein per kilo. The proportions were as follows:

	Calories Per Kilo	Proteins Per Kilo, Gm.
I. Vegetable Diet..............	80	3.0
II. House Diet..................	72	3.5
III. Milk Diet....................	55	2.6
IV. Animal Diet.................	70	5.0

The number of calories per kilo changed very little with the different diets excepting with the milk diet, because the children never took the amount required. The vegetable diet gave the greatest number of calories and the animal diet the greatest amount of protein per kilo.

As what I desired to determine in these experiments was the acid concentration of the urine, as well as the total acidity in twenty-four

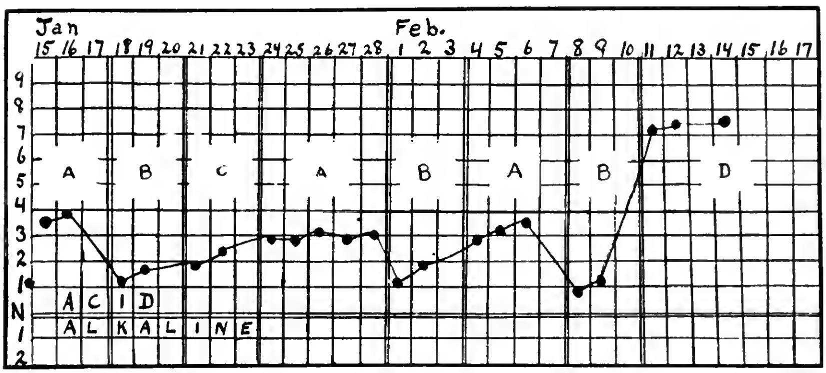

Chart 4.—Influence of diet on the reaction of the urine in a child aged 5½ years: *A,* house diet; *B,* vegetable diet; *C,* milk diet; *D,* animal diet.

hours, especial care was necessary in giving the children the same amount of water every day, because it is evident that with the same diet the total acid eliminated in twenty-four hours ought to be about the same; but the concentration of the same quantity of urine taken from the whole twenty-four-hour amount would vary with the total volume eliminated; in other words, with the amount of water ingested.

The curves in Charts 4 and 5 show the changes in the acidity of the urine in the two children on the four diets given. The acidity represented by the dots denotes the number of cubic centimeters of tenth-normal solution of sodium hydrate required to neutralize 10 c.c. of urine taken from the total twenty-four-hour amount.

The changes in the diets were made twenty-four hours before testing the urine.

The curves do not show as wide changes as in the babies, because the changes in the amount of protein in the diet could not be regulated as well. While in the babies the protein changed from 2 to 8 gm. per kilo, in these children they could be changed only from 2.6 to 5 gm. per kilo of body weight.

The two curves (Charts 4 and 5) are remarkable for their similarity, although with some minor differences. The first decrease after changing from the "house diet" to the vegetable diet, is wider in Curve 4 than in 5; and, on the other hand, the small increase after changing from the vegetable to the milk diet is more marked in Curve 5 than in 4. The noteworthy points in these curves are:

1. The acidity of the urine decreased on the vegetable diet and rose more and more on adding food of animal origin. This change is very noticeable in both curves between February 9 and 11, when the vegetable diet was changed to an animal diet.

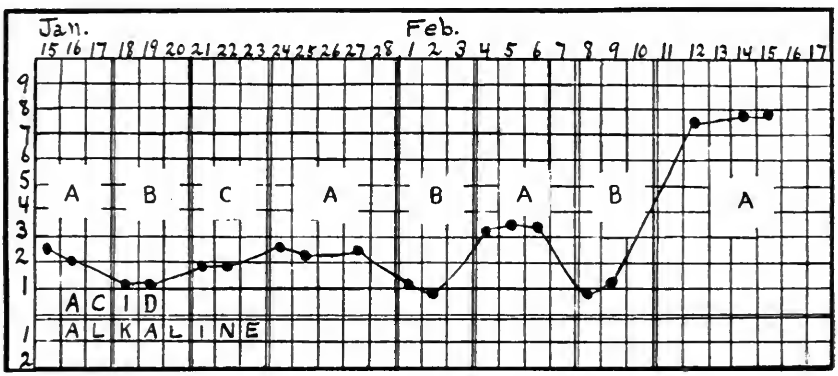

Chart 5.—Influence of diet on the reaction of the urine in a child aged 5 years: *A*, house diet; *B*, vegetable diet; *C*, milk diet; *D*, animal diet.

2. The difference in effect of the vegetable diet and milk diet was practically none. Theoretically, the acidity ought to increase with the milk diet (although not as much as with the animal diet), but the children only took on an average of 1,000 c.c. of milk daily, which only represented 2.6 gm. of protein per kilogram, being the smallest amount of protein taken during the experiment.

THE USE OF DRUGS

Only a superficial study was made of the drugs generally used to change the reaction of the urine, as it requires a great deal of time and hardly comes within the scope of this paper.

For making the urine acid, either acid sodium phosphate or sodium benzoate is generally used. The former is eliminated in its acid form

and the latter combines in the body with glycocoll, forming hippuric acid, which is excreted in the urine.

The curves representing the acidity and alkalinity of the urine as the result of the administration of drugs, do not represent the acidity or alkalinity of a fixed volume, but the acidity or alkalinity of each micturition, because in these experiments it was intended to study, not the daily changes, but rather the changes at frequent intervals during the twenty-four hours, on account of the fleeting action of the drugs.

Curve 6 shows that 2 grains (0.13 gm.) of acid sodium phosphate made the acidity increase to 12.5 c.c. It then decreased immediately after stopping the drug, reaching nearly the initial point (5.2 c.c.) eight hours after the last dose.

Curve 7 shows that the acidity remained the same for two hours after the first dose of 2 grains of sodium phosphate, which was probably due to a slower absorption, as three hours after the second dose the acidity rose from 2 c.c. to 14 c.c. As with the acid sodium phosphate, it dropped after the drug was stopped and reached 1.6 c.c. (a little under the initial point) eight hours after the last dose.

Curves 8 and 9 show that a single dose of 5 grains (0.33 gm.) of sodium benzoate had a similar effect, which began to diminish six hours after the dose had been administered.

From these experiments it seems conclusive that the acid sodium phosphate and the sodium benzoate must be given in frequent and repeated doses in order to maintain their action.

For making the urine alkaline potassium citrate or sodium bicarbonate is generally used. The indications for making a urine alkaline are more frequent in therapeutics than making it acid.

The following are two experiments which I think are worth mentioning:

One dose of 20 grains (1.25 gm.) of potassium citrate was given to a 5-year-old child with an ordinary "House Diet" to which about 15 gm. of extra meat were added. Then the same dose of the same drug was given while the child was taking a vegetable diet, adding as an extra, about 100 c.c. of orange juice (see Charts 10 and 11).

The results were that in the first part of the experiment the urine was acid and turned alkaline when the diet was changed.

The same experiment was made with the same diets, but giving 40 grains of sodium bicarbonate instead of the potassium citrate, and the same results were obtained (see Charts 12 and 13).

These last experiments are alike in results to those of the babies and demonstrate clearly the importance of the diet when it comes to changing the reaction of the urine.

Very often the potassium citrate and the sodium bicarbonate cause, especially in babies, digestive disturbances because of their action on the stomach. Such is the case in pyelitis and cystitis when one is

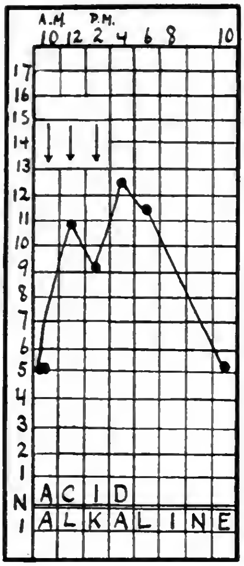

Chart 6

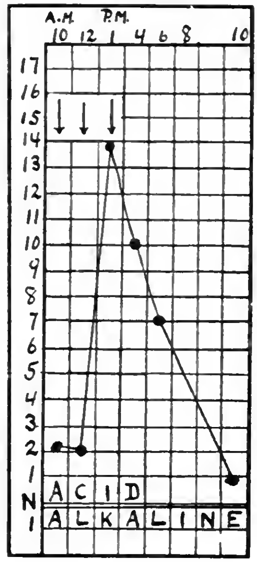

Chart 7

Chart 6.—Action of sodium acid phosphate in a child aged 5½ years, on a house diet. Arrows point to administration of 2 grains of the drug.

Chart 7.—Action of sodium acid phosphate in a child aged 5 years, on a house diet. Arrows point to administration of 2 grains of the drug.

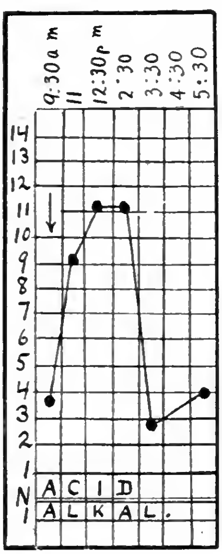

Chart 8

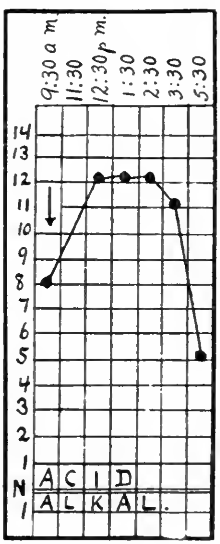

Chart 9

Chart 8.—Action of sodium benzoate in a child aged 5 years, on a house diet. Arrow points to administration of 5 grains of the drug.

Chart 9.—Action of sodium benzoate in a child aged 5½ years, on a house diet. Arrow points to administration of 5 grains of the drug.

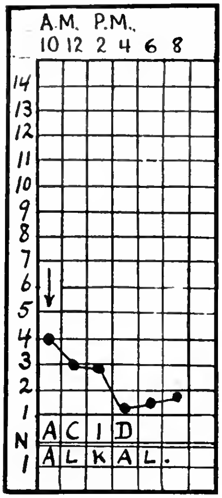

Chart 10

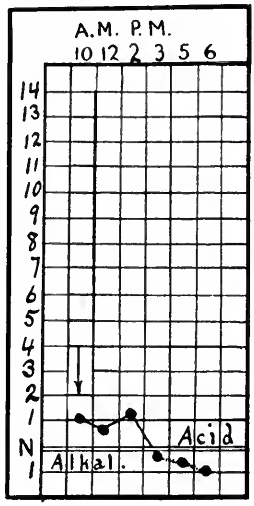

Chart 11

Chart 10.—Action of potassium citrate in a child aged 5 years, on a house diet. Arrow points to administration of 20 grains of the drug.

Chart 11.—Action of potassium citrate in the same child as in Chart 10, on a vegetable diet. Arrow points to administration of 20 grains of the drug.

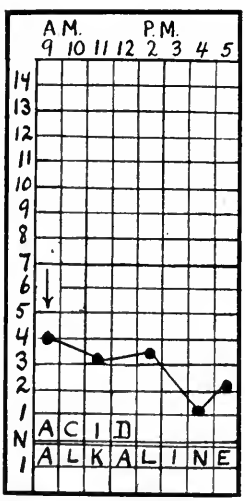

Chart 12

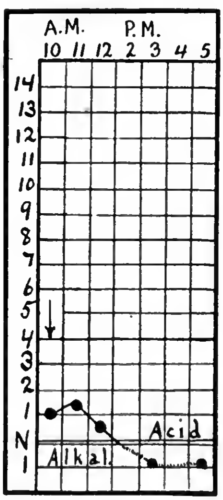

Chart 13

Chart 12.—Action of sodium bicarbonate in a child on a house diet. Arrow points to administration of 40 grains of the drug.

Chart 13.—Action of sodium bicarbonate in the same child as in Chart 12, on a vegetable diet. Arrow points to administration of 40 grains of the drug.

obliged to give very large doses of the drug. Hole has said: "The citrate of potash in this condition [pyelitis] is apt to cause diarrhea or vomiting. It is therefore wise to give no more than 5 or 10 grains."

The two following cases will illustrate this a little better:

S. M., 2½ months old, in the Massachusetts General Hospital with acute pyelitis, was fed on modified milk and a small amount of breast milk. He was treated in the beginning with hexamethylenamin, but on account of a suspicion of nephritis the treatment was changed to rendering the urine alkaline. For this purpose he was given 15 grains of potassium citrate every four hours.

After three days of this new treatment I examined the urine before the morning dose of the medicine was given, the acidity of which was 4.2 c.c.; in the evening, two hours after the third dose, the acidity was 1.2 c.c. By that time the baby had taken a little more than 1.11 gm. of potassium citrate per kilo, which is a larger dose than is ordinarily given, even when a large dose is intended.

The baby was getting in his food, 4.27 gm. of protein per kilo. Perhaps if the protein had been diminished the urine would have become alkaline, but I did not have the opportunity to follow up this case.

M. M., 2 years old, having pneumonia and laryngitis, following the removal of a foreign body from a bronchus, had pyelitis. In order to render the urine alkaline, she was given 30 grains of potassium citrate every 2½ hours.

The urine was examined in the morning, before the first dose, and the acidity was found to be 6.6 c.c., and after taking 120 grains of the potassium citrate it was still acid (4.3 c.c.).

It is evident from these cases how difficult it is to turn the urine alkaline, when there is an infection in the urinary tract, without regulating the diet according to the schemes described.

CONCLUSIONS

1. The difficulties which one often encounters in changing the reaction of the urine in children are very much diminished when a suitable diet is prescribed.

2. Diminishing the amount of protein in the diet to 2 gm. and sometimes to 3 gm. per kilo will often in itself render the urine alkaline without using a drug.

3. In cases in which the amount of protein reaches the lowest physiologic limit without turning the urine alkaline, one may continue to diminish the acidity by adding vegetables to the diet.

4. In older children with whom the food is more varied, one can do much by regulating the diet in accordance with the principles outlined in this article.

5. In cases in which vegetables are used to turn the urine alkaline, one must use, if possible, vegetables in which the amount of protein is smaller in proportion to the salts, like fruits, rice, wheat, etc., rather than those which have a large amount of protein like pease, beans, etc. Vegetables which contain purins, like coffee, tea and cocoa, may increase the acidity, because they may produce uric acid.

6. In cases of infection, especially in infections of the urinary tract, and in cases of starvation, the urine tends to become more acid than in other conditions; therefore it is more difficult to render it alkaline.

7. When drugs are used without the proper diet, the doses necessary to make the urine alkaline are much larger than is ordinarily believed.

8. The action of drugs (either acid or alkaline) is very fleeting; therefore they should be given in large and frequent doses.

I desire to express my gratitude and thanks to Drs. Fritz B. Talbot and Joseph I. Grover for the suggestions and assistance and for facilities provided for my experiments, the former physician in the Massachusetts General Hospital and the latter in the Infants' Hospital.

THE BANANA AS A FOOD FOR CHILDREN *

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AND
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The banana has been regarded as of doubtful value in the dietary of children, and it seemed worth while to investigate the merits of a food so abundant, economical and popular, and to determine the best ways of using it to get full nutritive value without digestive disturbances.

The chief food constituents of the banana are the carbohydrates which amount to about 22 per cent. In the green fruit these are in the form of a starch, but on maturing this is converted first into sucrose and finally into invert sugar. The proteins amount to less than 1 per cent. and their nature is at present unknown. The fat and fiber are negligible. The ash is important both in amount and kind of its constituents. Fruits are generally recommended for their vitamin content, and it is reasonable to think that the banana may have its share. These dietary accessories or vitamins are at present being investigated. The main value of the fruit lies, then, in its carbohydrates, ash, and possibly its accessories. The composition of the banana is compared with that of some other common fruits and the potato in Tables 1 and 2. The figures in these tables refer to the edible portion of the fresh food.

While theoretical considerations and practical tests made in this institution show that the banana is a valuable food, it is not to be regarded as a complete food in itself or to be recommended as the sole or main part of a child's diet. It cannot take the place of such staples as milk, cereals, or potatoes, though it may in part replace the latter two at times. When *fully ripe* it is a good fruit for children and may be given freely without danger or harm except as it may crowd out other foods more essential for growth. *The underripe uncooked fruit should never be given to children. Bananas that are merely yellow are not ripe.* Characteristic changes take place in the peel as the fruit matures. The thick, turgid covering of the green banana becomes thinner and more pliable, the color passes from green

* Submitted for publication July 24, 1917.

* From the Department of Pediatrics and the Laboratory of Pathological Chemistry, New York Post Graduate Medical School and Hospital.

TABLE 1.—COMPARATIVE COMPOSITION OF SOME COMMON FRESH FRUITS AND POTATOES *

Fruit	Protein	Carbohydrate	Calories per Pound	Grams Required to Yield 100 Calories
Banana	1.3	22.0	447	101
Grapes	1 3	19.2	437	104
Plums	1.0	20.1	383	118
Cherries	1.0	16.7	354	128
Raspberries	1.7	12.7	290	150
Pears	0.6	14.1	288	158
Apples	0.4	14.2	285	159
Blackberries	1.3	10.9	262	173
Apricots	1.0	13.4	247	172
Orange	0.8	11.6	233	195
Peaches	0.7	9.4	187	242
Pineapples	0.4	9.7	197	233
Lemons	1.0	8.5	201	226
Cantaloup	0.8	9.3	180	252
Strawberries	1.0	7.4	177	269
Watermelons	0.4	6.7	136	332
White potatoes	2.2	18.4	378	120
Sweet potatoes	1.8	27.4	558	81

* Olives, sweet potatoes, and corn are the only common fresh fruits and vegetables that have a higher fuel value than the banana. Other fruits and vegetables that may be classed with the banana as having approximately 1 calory per gram are grapes, plums, and potatoes as given above, together with figs, which are almost identical with bananas, and dates with a fuel value equal to that of the grapes. This table is compiled from data taken from Rose, M. D. S.: Laboratory Handbook for Dietetics, New York, and was used in part in a former paper: Myers and Rose: Jour. Am. Med. Assn., 1917, **68**, 1022.

TABLE 2.—ASH CONSTITUENTS OF SOME COMMON FRUITS *

Fruit	Ash Constituents of Fruits in Percentage of the Edible Portion							
	CaO	MgO	K_2O	Na_2O	P_2O_5	Cl	S	Fe
Bananas	0.01	0.04	0.50	0.02	0.055	0.20	0.013	0.0006
Grapes	0.024	0.014	0.25	0.03	0.12	0.01	0.024	0.0013
Plums	0.025	0.02	0.25	0.03	0.055	0.01	.....	0.0005
Cherries	0.03	0.027	0.26	0.03	0.07	0.01	.....	0.0005
Pears	0.021	0.019	0.16	0.03	0.06	....	.....	0.0003
Apples	0.014	0.014	0.15	0.02	0.03	0.004	0.005	0.0003
Oranges	0.06	0.02	0.22	0.01	0.05	0.01	0.013	0.0003
Peaches	0.01	0.02	0.25	0.02	0.047	0.01	0.01	0.0003
Lemons	0.05	0.01	0.21	0.01	0.02	0.01	0.012	0.0006
Muskmelons	0.024	0.02	0.283	0.082	0.035	0.041	0.014	0.0003
Strawberries	0.05	0.03	0.18	0.07	0.064	0.01	.....	0.0009
Watermelons	0.02	0.02	0.09	0.01	0.02	0.01		
White potatoes	0.016	0.036	0.53	0.025	0.14	0.03	0.03	0.0013
Sweet potatoes	0.025	0.02	0.47	0.06	0.09	0.12	.....	0.0005

* Sherman, H. C.: Chemistry of Food and Nutrition, p. 332.

to pale yellow, deepening to golden yellow with brown spots, and finally becoming brown all over. Bananas are edible raw when the brown spots appear and need not be refused as overripe when the peel is entirely brown if the covering is intact and the pulp shows no signs of fermentation. The brown color of the ripening must not be confused with the brown patches due to bruising (Table 3).

TABLE 3.—Changes Taking Place in the Banana During the Process of Ripening *

Days off Boat	Per Cent. of Peel	Reducing Sugar in Terms of Glucose, per Cent.	Sucrose in Terms of Glucose, per Cent.	Total Sugar in Terms of Glucose, per Cent.	Remarks on the Condition of the Peel and Pulp
2	40	0.6	1.2	1.75	These bananas were very green and firm; could be handled like cord-wood without harm to fruit; the peel adheres to pulp; total carbohydrates about 22 per cent.
4	39	1.2	4.6	5.8	Greenish yellow with pea green edges; peel still adheres to pulp; taste bitter and astringent; starch about 15.5 per cent.; may be baked at this stage, but preferable to hold until two days later
6	36	2.9	12.5	15.4	Yellow except at extreme edges and tip; there is a beginning of the golden tints; the peel does not adhere to the pulp; the bitter taste has largely disappeared; starch about 7.5 per cent.; very good for baking
8	32	4.1	11.9	16.0	Greenish cast to edges; otherwise a full yellow; starch 5 per cent.; flavor somewhat herbaceous: this fruit should not be eaten raw though it is frequently consumed at this stage
12	26	5.4	11.7	17.1	Golden yellow with some suggestion 1 green on edges and tip; few brown specks; herbaceous flavor: this fruit may be eaten raw by adults but it is preferable to hold it over one more day before serving to children
14	26	6.9	11.7	18.5	Full golden yellow with many small brown spots; starch 3 per cent.; flavor delightful; perfectly safe to consume this fruit in any reasonable quantities
15	26	7.1	11.1	18.8	Extensive patches of light brown; starch less than 1 per cent.; excellent flavor and mellow texture; at optimum condition for eating raw

* The above figures and remarks are based on a bunch of bananas received from a refrigerant boat in November. The course of the ripening process is influenced by the temperature, and different data would be recorded from a bunch examined in the summer months. In warm weather the pulp advances more rapidly than the peel and a banana in a golden yellow skin may be as mellow as the light brown fruit.

To establish clearly the true nutritive position of the banana, a large number of carefully controlled feeding experiments have been conducted on normal adults, invalids and children, including infants. The fruit has been used in various degrees of ripeness. It was impossible to feed the raw banana in the early stages of yellowing on

account of the bitter astringent still present. Fruit of this ripeness, however, served to adults and children, baked in the skin as in baked potatoes, and mashed with butter before eating, proved quite acceptable.[1] The underripe banana when baked is utilized to about the same extent as the potato and is similar to this vegetable in its nutritive value. There was in no case any suggestion of deleterious effects from eating the banana baked or raw when fully ripe.

In the late yellow stage, before the development of the distinct golden color, the raw fruit can be consumed by normal individuals in small quantities (say one or two bananas) without discomfort or apparent harm. Nevertheless the authors are of the opinion that the raw fruit should not be given to children at this stage. In one instance, where the plan was to have the banana at this stage of ripeness as the sole food for three days, a distinct disturbance developed after the fifth meal, manifesting itself in nausea and vomiting. It should be added, however, that 1.5 kg. had been taken without any uncomfortable feelings whatever before the symptoms manifested themselves. No such symptoms have been produced by the fruit in the golden yellow stage of ripeness. Several adults were kept on a diet consisting almost exclusively of milk and fully ripe bananas for periods of a week. For example, in one case the diet was composed of 1,000 gm. banana, 1 quart of milk, and 1 cup sweetened coffee per day for one week. The experience was one of comfort, satisfaction, and unimpaired efficiency, and the diet was more pleasurable than that of a similar period in which the banana was replaced by its calorific equivalent of fresh white wheat bread. The utilization of the banana carbohydrate in these cases was 98.8 per cent.

The experiments on children consisted in feeding carefully controlled dietaries planned to be adequate and normal in every way. These were divided into periods of from three to seven days. "Control" periods in which no banana was served were either made up of the regular ward diet or of a similar vegetarian diet. In the latter case the same diet was repeated each day of the period. Very underripe bananas were excluded, as these are known to be unsuitable. In the "banana test" period the banana was introduced as a substitute for the more starchy foods, such as cereals and potato, and ranged in amount from one small banana to three-quarters of the day's carbohydrate quota. With one exception the banana was mashed to prevent the child from bolting it in unmasticated lumps. The food served was weighed on a Harvard trip scales to within 1 gm. and when it was not

1. The banana may be baked at all stages, even when very green, but the pulp of the banana baked before the peel has assumed the yellow color becomes tough and dry. The green banana is desiccated and ground into a meal in which form it is sometimes used.

all eaten the returned parts were also weighed and recorded. The stools were collected quantitatively and analyzed. The reaction to litmus and reduction of picric acid were employed to detect any signs of intestinal fermentation. The determinations of carbohydrates were made by the modified picric acid method.[2] The reduction of picric acid after acid hydrolysis, expressed in terms of glucose, is assumed to represent the starch and dextrin of the stools. The total carbohydrate thus determined in the stools subtracted from the ingested carbohydrates gives the apparent utilization of this food element and is expressed in terms of per cent. of the carbohydrate consumed. The foods used were not themselves analyzed but calculated from tables used in planning the diets.[3]

The nurses in charge of the children were interested in the experiments and gave a hearty cooperation in the work. The probable errors, therefore, were reduced to two; that of obtaining food surreptitiously, which would weight the balance against the banana, and secondly the loss of stools, which would weight the balance in favor of the banana; but, on the other hand, loss of stools would be certain of detection by both the magnitude of the deflection from the mean daily carbohydrate elimination and the conflict with the recorded defecation habit. Most of the known and suspected mishaps have been ruled out by eliminating the cases from further consideration or in the cases in which they have been included in this study by omitting the defective days from the calculations.

DATA FROM THE EXPERIMENTS

The reliable data from these experiments are briefly reviewed in the following:

Case 1.—A. R., aged 5 years, girl, weighing 35.6 pounds. Rheumatic endocarditis; constipated, requiring enema and purgatives before and after the test, also during the test. The diet before the test was described as "soft." There were two control periods consisting of farina, bread, butter, oatmeal, potatoes, soup, milk, and cocoa. In two other periods the potato and part of the cereal were replaced by bananas, mashed in the one period and thickly sliced in the other. The banana was partly golden yellow, but not yet darkened or spotted with brown specks. There were, therefore, unaltered starch grains left in the pulp. The subject took the meals as well as could be expected and no mishaps occurred except on the last day when a distaste for the foods developed and the noon meal was regurgitated. This day is not included in the numerical data of Tables 4 and 5.

Case 2.—F. C., aged 6 years, boy. Congenital malformation; mentally subnormal; parentage and history unknown; laboratory findings and observations indicate physiologic normality. This subject was on the test at the same time as Case 1 and the same diet and management of details were employed. No vitiating factors are known. These two cases were the first cases used in

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2. Myers, V. C., and Bailey, C. V.: Jour. Biol. Chem., 1916, **24**, 147.

3. Rose, M. D. S.: Laboratory Handbook for Dietetics, New York, 1912; and Feeding the Family, New York, 1916.

the baby ward for this study and were very closely watched by all concerned. The numerical data relating to them are tabulated in detail as illustrative of the whole plan and the following cases are presented more briefly (see Table 4).

TABLE 4.—NUMERICAL DATA PERTAINING TO CASES 1 AND 2

	Case 1				Case 2		
	Control Period May 4-7	Banana Period May 8-11	Control Period May 12-15	Banana Period May 16-18	Control Period May 4-7	Banana Period May 8-11	Control Period May 12-15
Carbohydrate intake, gm. .	210	320	210	320	210	320	210
Amount of feces, gm.	221	306	260	247	228	200	173
Reducing substances in the feces after acid hydrolysis in terms of glucose, per cent.	1.44	2.8	1.2	2.83	1.8	2.5	1.5
Estimated amount of carbohydrate in the feces in terms of glucose, gm. ..	3.1	8.6	3.2	7.0	4.1	5.6	2.6
The apparent utilization of the carbohydrates in per cent. of the carbohydrates ingested	98.5	97.3	98.7	96.8	98.1	98.3	98.8

CASE 3.—R. P., aged 3 years, girl, weighing 21.6 pounds. Congenital syphilis. The Wassermann test was negative. The stools were mostly normal and regular. During the stay in the hospital the bowels failed to move seven days, three of which were due to an attack of constipation prior to the test and three to an attack during the test. The appetite was good and all meals were taken regularly throughout. The control period of five days was based on a daily diet consisting of farina 80 gm., bread and butter 120 gm., potatoes 60 gm., rice pudding 100 gm., 1 egg, 1 baked apple, 100 c.c. soup and 400 c.c. milk. The banana test diet was the same, with the substitution of ripe bananas for 60 gm. of the cereal, and all of the rice, potatoes, and apples in calorifically equivalent amounts. The carbohydrate in the stool varied very little from day to day and for the control period averaged 0.71 gm. and for the banana days, 0.77, indicating practically complete utilization.

CASE 4.—R. S., aged 5½ years, girl weighing 40.56 pounds. Convalescent from typhoid fever; constipated; required frequent enema; vomited; abdominal pains both before and during the experiment. The diet used was the same as that in Case 3. Several stools were lost. For those days of the test when the control of the experiment was reasonably good the average of the carbohydrate in the stools was 0.11 gm. for the banana days and 0.15 and 1.2 gm. for two of the control days. The unusually low elimination of carbohydrate corresponds to days of unassisted defecation, yielding very firm stools; the higher figure represents three days of enema treatment.

CASE 5.—D. C., aged 6½ years; boy weighing 33 pounds. Tuberculosis of the ankle; constipated, but the stools were regular during the experiment. This child's appetite was subnormal. In the control period the regular ward diet was employed, the following being a sample day: cereal 140 gm., milk 550 c.c., meat 10 gm., potatoes 40 gm., apple sauce 30 gm., and broth 150 c.c. There were two periods in which banana replaced part of this regular diet; in the one 200 gm. of banana were prescribed and in the other 400 gm., the other food being left to the choice of the patient and the nurse; but the quantities actually consumed were weighed and recorded. An insufficient amount of food was taken in all of the periods, the lowest being in the control period

in which only 800 calories or about one-half of the normal amount was taken. In the banana periods the calories were brought up to 1,000. The amounts of carbohydrate in the stools of the control period were unusually uniform from day to day, varying less than 0.4 gm., with an average for the period of 2.50 gm. In the 200 gm. banana period the carbohydrates in the stools averaged 2.93 gm., or a trifle more than that of the control period, but more carbohydrate was consumed. In the last period, 400 gm. banana, the carbohydrate in the feces came to only 0.9 gm. There was a higher calorific intake than in the control period but also less bread and cereal than in either of the other two. The bananas used in this case and in Case 6 were very ripe. The peel was allowed to assume a dark brown color before the fruit was served and would be considered too ripe by most persons. The flavor of these bananas was excellent.

Case 6.—N. G., aged 3 years, boy weighing 25 pounds. Arthritis of the right ankle. The bowel movements and stools were normal throughout the test. This subject paralleled Case 5 and the same routine was followed. The patient was discharged before the last period could be completed. The appetite of this boy was very good and he consumed his full required quota. The average carbohydrate content of the feces for the control period was 1.2 gm. per day and for the 200 gm. banana days, 2.16 gm. More carbohydrate was consumed in the latter period than in the former.

Case 7.—L. C., aged 3 years, boy weighing 27.6 pounds. Empyema. The stools contained a large number of segments of tape worm (*Saginata*); they were frequent, soft, and bulky. The stool of March 24, was bloody. There were no stools voided April 17 and 22. At the end of the first day an enema was given; no treatment for the omission of defecation on the 22d; two stools voided on the 23d. At no time was there constipation and no stools from this patient were firm or well formed. The regular ward diet was used as the basal ration and the banana was added to this in place of some of the cereal and potato. The boy had an unusual appetite and desired more food than was allowed during the test. At no time was there any discomfort attributable to the diets. The bananas used were very ripe. There were three banana test periods. One day's dietary in the last period was the following: 7 a. m., cream of wheat 50 gm, bananas 100 gm., milk 200 c.c.; 10:30 a. m., bread and butter 1 slice, milk 200 c.c.; noon, cream soup 100 c.c., bread and butter 1 slice, bananas 200 gm., milk 200 c.c.; 3 p. m., bread and butter 2 slices; 5:30 p. m., bread and butter 1 slice, bananas 100 gm., milk 200 c.c. This gives approximately 1,500 calories for the day, of which nearly 26 per cent. is derived from the banana. Period of April 11-15: 200 gm. of bananas were consumed per day and 996 gm. of feces were voided with a carbohydrate content of from 3.2 to 8 per cent., and averaging 5.75 gm. per day. Period April 16-20: 150 gm. of bananas were consumed per day and 534 gm. of feces voided with a carbohydrate content of 1.52 to 3.21 per cent. The stool for the 18th was very soft and that for the 19th liquid. The stool for the 20th, which was almost liquid, reacted acid to litmus, one of the very few acid stools of the whole series of experiments. The average amount of carbohydrate eliminated in these stools was 1.85 gm. per day. This figure is low in comparison with the others of this test and it must be assumed that there was an appreciable loss through fermentation of the fecal matter. There was also a suspicion at the time the feces were collected and analyzed that there had been a loss of stool wholly or in part, but no evidence to this effect could be obtained. Period of April 21-27; control period; no bananas were served. The child was allowed to eat freely of the regular ward diet. The stools were not as soft as those of the preceding periods. The percentage of carbohydrate in the stool ranged within narrower limits, 1.58 to 1.77. The average daily elimination of carbohydrate in the feces was 1.35 gm. Period of April 28 to May 7: 400 gm. bananas were given. The amount of carbohydrate in the stools was irregular, varying from 1.07 to 3.2 per cent. There were five very

soft stools for the first two days; the subsequent stools were more normal in appearance. The lower per cent. of carbohydrate in the stools fell in the middle of the period. The daily average carbohydrate elimination for this period was 2.55 gm. This case is included in the report because it gives a very different impression from all of the others, one less favorable to the banana. The tapeworm is in this case a disturbing factor in the interpretation of the analytical results, as we can have no assurance that its glycogen content is evenly distributed throughout the sample, and the segments of the parasite were far from being uniformly passed in the stools.

Case 8.—F. T., aged 2 years, boy weighing 28 pounds. Acute bronchitis. The control diet consisted of farina, bread, butter, potatoes, rice, egg, apple, cream, and milk. The carbohydrates ingested each day came to 120 gm. Four days constituted a period. The banana period had baked underripe and raw ripe bananas, besides the same amount of bread and butter as in the previous period, and an extra portion of butter which was worked into the mashed baked banana. The milk in this second period was the same as before; the cream was doubled. This period gave 140 gm. of carbohydrate, 30 derived from baked bananas and 75 gm. from raw bananas. All the food prescribed was taken and the child was well satisfied with his meals. There was no evidence of discomfort or disturbance of any kind. The stools were soft and yellow and defecations regular. The carbohydrate in the stools was remarkably constant, from 0.75 to 0.81 gm. per day. The lower figure fell within the control period. The apparent utilization of the banana was better than 99 per cent.

Case 9.—M. S., aged 3½ years, girl weighing 25.25 pounds. Osteo-arthritis (arthritis deformans). This experiment was synchronous with and similar to that in Case 8, with practically identical results.

Case 10.—G. B., aged 4½ years, boy weighing 30.75 pounds. Enlarged bronchial lymph nodes. The control diet consisted of farina, bread, butter, soup, egg, potatoes, cream, and milk. These were given to the subject for the days February 18 to 21 and March 10 to 13. Ripe raw bananas were given with this control diet from February 22 to March 9, and baked underripe bananas replaced the raw bananas from March 14 to 16. There was an interference with the experiment in that calomel and salts were administered from March 8 to 11. During this time the stools were frequently liquid and decidedly reducing to picric acid before acid hydrolysis. The estimated carbohydrates for the stools for these days indicated a carbohydrate elimination of from 4 to 8 gm. per day, consisting almost entirely of reducing sugars. Following this period of purgation the fecal carbohydrate dropped to 1.56 gm. per day for the remainder of the control period and to 1.28 gm. for the banana period. All of these stools were soft and at times almost liquid. The stools prior to the calomel treatment were of firm consistency and in the control period yielded only 0.6 gm. carbohydrate per day, and in the banana period from 0.4 to 1 gm.

Case 11.—H. S., aged 4½ years, girl weighing 34 pounds. Acute parenchymatous nephritis. The determination of the nitrogenous waste products in the blood of this patient gave high figures within the limits accepted as normal. The patient was later discharged as cured. Constipated; nearly all stools followed either enema or suppositories. The diet prior to the test was restricted as to salt and fluids; otherwise like the regular ward diet. The appetite was subnormal. The following was the menu for the first four days: morning, farina 60 gm., ripe raw bananas 100 gm., cream 1 tablespoonful, and 200 c.c. milk; noon, baked underripe bananas 75 gm., cocoa 200 c.c., steamed rice 60 gm.; evening, ripe raw bananas 100 gm., cream 2 tablespoonfuls, and milk 200 c.c. The second period of four days was the same, with baked potatoes in place of the baked bananas. In the third period the ripe bananas were also omitted, and bread and butter given in their place, the rice being

replaced by cabbage and lettuce. The total daily amount of carbohydrate in the feces for these periods came to 0.5, 1.4, and 1.8 gm., giving no excess attributable to the banana.

TABLE 5.—A SUMMARY OF THE NUMERICAL DATA IN THE DIGESTION EXPERIMENTS ON BANANAS WITH CHILDREN AS SUBJECTS

Case	Period	Carbohydrate Intake, Gm.	Carbohydrate in the Feces, Gm.	Apparent Utilization of the Carbohydrate, per Cent.	Remarks
1	Control.............	210	3.1	98.5	Yellow bananas used, sliced in last period
	Banana.............	320	8.6	97.3	
	Control.............	210	3.2	98.7	
	Banana.............	320	7.0	96.8	
2	Control........	210	4.1	98.1	Same as in Case 1
	Banana.............	310	5.7	98.3	
	Control.............	210	2.6	98.8	
3	Control.............	142	0.7	99.5	Brown spotted bananas
	Banana.............	147	0.8	99.5	
4	Control.............	142	0.1	99.0+	
	Banana.............	147	0.2	99.0+	Same as Case 3
5	Control.............	90 ?	2.6	97.2 ?	
	Banana.............	120 ?	2.9	97.7 ?	Golden yellow bananas
	Banana.............	130	0.9	99.3	Brown spotted bananas
6	Control.............	992	1.2	98.6	
	Banana.............	120	2.2	98.2	Brown spotted bananas
7	Control.............	120	1.4	98.9	
	Banana.............	...	1.9	....	Fully ripe bananas in the three periods but different amounts
	Banana.............	...	5.8		
	Banana.............	154	2.6	98.3	
8	Control.............	120	0.9	99.3	
	Banana.............	140	0.7	99.5	Baked bananas
9	Control.............	120	0.8	99.4	Baked bananas
	Banana.............	140	0.8	99.4	
10	Control.............	120	1.6	98.7	
	Irregular.............	120–131	4.0-8.0	93.5–97.0	Purgatives given
	Banana.............	131	1.3	99.0	Brown spotted bananas
	Banana.............	124	1.0	99.2	Baked bananas
11	Control.............	120	1.8	98.5	Baked potatoes
	Banana.............	124	0.5	99.6	Baked bananas
	Banana.............	131	1.4	98.8	Brown spotted bananas

For more convenient comparison of the material in these studies the numerical data have been arranged in tabular form (Table 5). The essential factors are the amount of carbohydrate intake and the amount of carbohydrate output in the stools, shown in the first two columns of numbers. The third column gives the calculated proportion of ingested carbohydrate not accounted for in the feces. The difference between the amount in the stools and that consumed is commonly considered as that which has been assimilated and used by the organism. Since the carbohydrates of the banana are compared with other vegetable foods fed under identical conditions, this apparent assimilation may reasonably be supposed to give a true criterion of the nutritive value of the banana.

Feces contain small amounts of substances which may reduce picric acid after hydrolysis other than those derived from the carbohydrates of the food, but these are so nearly negligible that they may for the present be left out of consideration and the total reduction charged against the unassimilated carbohydrates. In the cases that have been studied the difference between banana and the foods with which it has been compared are very small indeed and in most instances to the advantage of the banana. In the first two cases the bananas used were in the late yellow stage of ripeness; that is, they did not have the full golden tint or any browning on the peel. Such bananas are usually considered ripe and possess the favorite flavor. The fruit at this stage does not give the blue color reaction when treated with iodin, but by careful teasing and with the aid of the microscope starch can easily be demonstrated as present. Microscopic examination of the stools of these two children revealed starch grains. From theoretical considerations one would expect somewhat lower utilization of the carbohydrates than the data indicate, possibly some raw starch being converted into its simpler components in the intestines. In all of the following cases the banana when fed raw was fully ripe; that is, there was no trace of the greenish cast to the yellow of the peel and there was at least a beginning of the brown coloration. In cases 7, 8 and 9 the bananas were decidedly brown and considered over ripe and unfit by the maids of the hospital. The almost complete utilization of these is apparent from an inspection of the table. There is a more complete assimilation in cases of constipation than when the bowels are loose. This is made evident by comparing 3 and 4 with 7, and the days of violent purgation with the normal days in Case 10. Most of the children were constipated. There was no positive evidence brought out that the banana as such was the cause of constipation any more than any other carbohydrate food, and in only two instances (including the one reported in this paper, 7) is it suggested that the banana may have the opposite effect. The impression of the physicians who observed the cases in the ward was that the banana test meals tended to produce a condition of constipation.

Baked bananas have been fed to adults and their apparent utilization compares well with that of the baked potatoes, being over 98.5 per cent. Baked bananas both from the green and the early yellow stage were fed to Patients 8, 9, and 11 of this series and compared with both raw ripe bananas and with the control foods, including baked potatoes, showing somewhat better utilization than the raw bananas and the other foods; but the differences were always so slight as to be practically negligible.

There was no evidence that the feeding of raw ripe bananas in large amounts for periods up to two weeks caused any deleterious

effect on a young child. The periods were too short to show much influence on the weight, though in Case 7 there was a small gain. In only one case was there any disturbance that might be attributed to the banana. This was Case 1, a delicate, shy, Italian girl who was not very fond of the fruit. Though very tractable and friendly to those in charge she would not admit a distaste for the banana until the end of the experiment. In the fourth period the bananas were fed in thick slices instead of mashed, as was otherwise done, to see whether poor mastication would decrease the utilization of the carbohydrates. A slightly lower utilization is indicated by the analytical data. The last noon meal was regurgitated about one-half hour after eating and in the regurgitate were lumps of the banana. No other symptoms devoloped and the child seemed in as good a condition as ever. It should be noted that in this period the bananas were in the stage of late yellow before the development of the full golden tint or before the beginning of the brown spots.

Bananas were also given to a child younger than any of those reported above. This was a mongolian idiot that would not take his meals voluntarily. The child was 19 months old and fed largely on milk and semiliquid food. He was kept on milk and baked bananas for eleven days and on nothing but ripe raw bananas for another ten days. The amount of bananas which the nurse could get into this child ranged from 175 gm. to 550 gm. a day. When milk was prescribed none was consumed on several days and the most taken without loss through regurgitation was 225 c.c. It was easier to get this boy to take the bananas than any of the other foods offered. There were no unfavorable results from the exclusive ripe raw banana diet.

SUMMARY

The banana is a useful fruit that can with profit enter liberally into the child's dietary provided it is fully ripe or well cooked. If eaten baked in the yellow stage of ripeness or if eaten raw when fully ripe, the banana makes a delightful and highly nutritious article of food. Its composition does not warrant the use of the banana as the main component of the child's dietary, but it can compete well with other fruits and is decidedly to be preferred to candies. The nutritional value is relatively high, approximately one calory per gram of pulp; and its carbohydrates, when it is fully ripe or cooked, are not less assimilable than those of cereals and potatoes. In the raw food the digestibility is directly proportional to the ripeness of the fruit. There is no positive evidence that the banana influenced bowel movements. In the many tests there was no suggestion whatever of any deleterious effect from consuming large amounts of fully ripe bananas. Prolonged use of the underripe fruit, on the other hand, developed

undesirable symptoms. Ripeness can be readily determined by the color and texture of the peel as indicated by Table 3. In ripening, the peel changes in color from its original deep green to a dark brown. In this change the color of the banana passes through several yellow stages which are generally taken to be signs of ripeness, but a yellow banana is not necessarily a ripe banana and if consumed raw while it still has a green cast to the yellow color, as is frequently done by children on the streets, the availability of its carbohydrates is comparatively low and the effect on the child's digestive system injurious. The banana ought not to be eaten raw until after the brown spots begin to appear. It is at this stage a full golden yellow and in its most attractive appearance. A completely browned skin is not in itself a sign of overripeness and such fruit should be judged by the texture of the pulp. The brown color of the peel, however, should not be confused with the darkening due to bruises. An injured banana is soon invaded by moulds and yeast cells both through the abrasions and the broken end, so that the banana "finger" should not be broken from the "hand" or stem but cut off in such manner as to leave a good margin between the cut surface and the pulp. The banana properly handled and allowed to ripen to its most beautiful color and texture is a wholesome food, uncontaminated by dirt and pathogenic germs even if purchased from the push cart in our congested streets.

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THE DIAGNOSIS OF THE AGE OF THE FETUS BY THE USE OF ROENTGENOGRAMS *

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The determination of the age of the fetus is of considerable practical importance. On the age of the fetus and on its development are based the chief factors that are to be considered before giving prognosis as to the possibility of saving the life of the prematurely born infant. The method of treatment, and especially that of feeding, depends primarily on the age of such infant. In medicolegal cases the question of the age of the fetus may occasionally be of paramount importance, and when only portions of the fetus are available for examination, the roentgenographic method offers the best means for arriving at a diagnosis of the age of such fetus.

Time of Conception.—The age of the fetus is the time which has elapsed from conception; that is, from the time of the fertilization of the ovum from which the fetus developed. The time of conception cannot be accurately determined. Conception does not follow immediately after insemination, and its relation to menstruation is so uncertain that an error of one month is possible in attempts to calculate the age of the fetus from the time of menstruation. A number of observers, Arnold,[1] Bischoff,[2] Dalton,[3] Leopold and Mironoff,[4] Leopold and Ravano,[5] and Reichert[6] have found that menstruation and ovulation usually occur at the same time, but that ovulation may take place at

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1. Arnold: Inaug. Dissert., Würzburg, 1887.
2. Bischoff: Beweis der von der Begattung unabhängigen periodischen Reifung und Lösung der Eier der Säugetiere und des Menschen als erste Bedingung ihrer Fortpflanzung. Giessen 1844. Entwickelung des Hundeeies, 1845.
3. Dalton: The Corpus Luteum of Menstruation and Pregnancy. Philadelphia, 1851.
4. Leopold and Mironoff: Arch. f. Gynäk., 1894, **14.**
5. Leopold and Ravano: Arch. f. Gynäk., 1907, **83.**
6. Reichert: Beschreibung einer frühzeitigen menschlichen Frucht im blasenförmigen Bildungszustande. Abhandl. d. k. preuss. Akad. d. Wissensch., Berl., 1873.

any time during the intermenstrual period and that, on the other hand, menstruation may occur without ovulation.

Issmer[7] found that when pregnancy was calculated from the first day of the last menstruation it averaged 280 days in 1,220 cases, while in 628 cases it averaged 269 when estimated from a fruitful copulation.

Mall,[8] in his studies on the determination of the age of human embryos and fetuses, comes to the conclusion that "the most probable time of conception is during the first week after the menstruation, as advocated by Hensen[9] and other obstetricians, and that in determining the age of human embryos it is probably more nearly correct to count from the end of the last period, for all evidence points to that time as the most probable at which pregnancy takes place."

His conclusions are also confirmed by recent observations of Siegel[10] on 100 pregnant women in whom the day of an isolated intercourse could be determined, this being made possible by the conditions during the present war. He concludes that conception can only take place during the first twenty-one days after the last period, and that the most susceptible time is before the sixth day. In no case could conception be established after the twenty-first day, so that he thinks it is safe to say that the postmenstrual period is the most favorable time for fertilization.

According to all this, therefore, conception in most cases occurs shortly after menstruation, and the age of the fetus is to be counted from the last day of menstruation. But even using this method of computing the age, there is room for an error in some cases which may amount to as much as one month.

Length of the Fetus.—If the date of the last menstruation or the date of a single isolated coitus is not known, then estimation of the age has usually been made on the basis of the length of the fetus, which has been generally regarded as the safest guide in the determination of the age.

The average lengths of normal fetuses as given by different authors are shown in Table 1.

Issmer[7] estimated the length of pregnancy and the age of the child in a number of cases and gives the figures in Table 2 as to the length and the age of the baby.

The same author (Issmer) has observed that in children of the same length differences of ten to eighteen days in pregnancy are possible.

7. Issmer: Ueber die Zeitdauer der menschlichen Schwangerschaft. Arch. f. Gynäk., 1887, **30,** 277 and 1889, **35,** 310.

8. Mall. Keibel-Mall: Manual of Human Embryology, **1,** 196.

9. Hensen: Hermann's Handbuch der Physiologie, 1881, **6.**

10. Siegel: Deutsch. med. Wchnschr., 1915, No. 2.

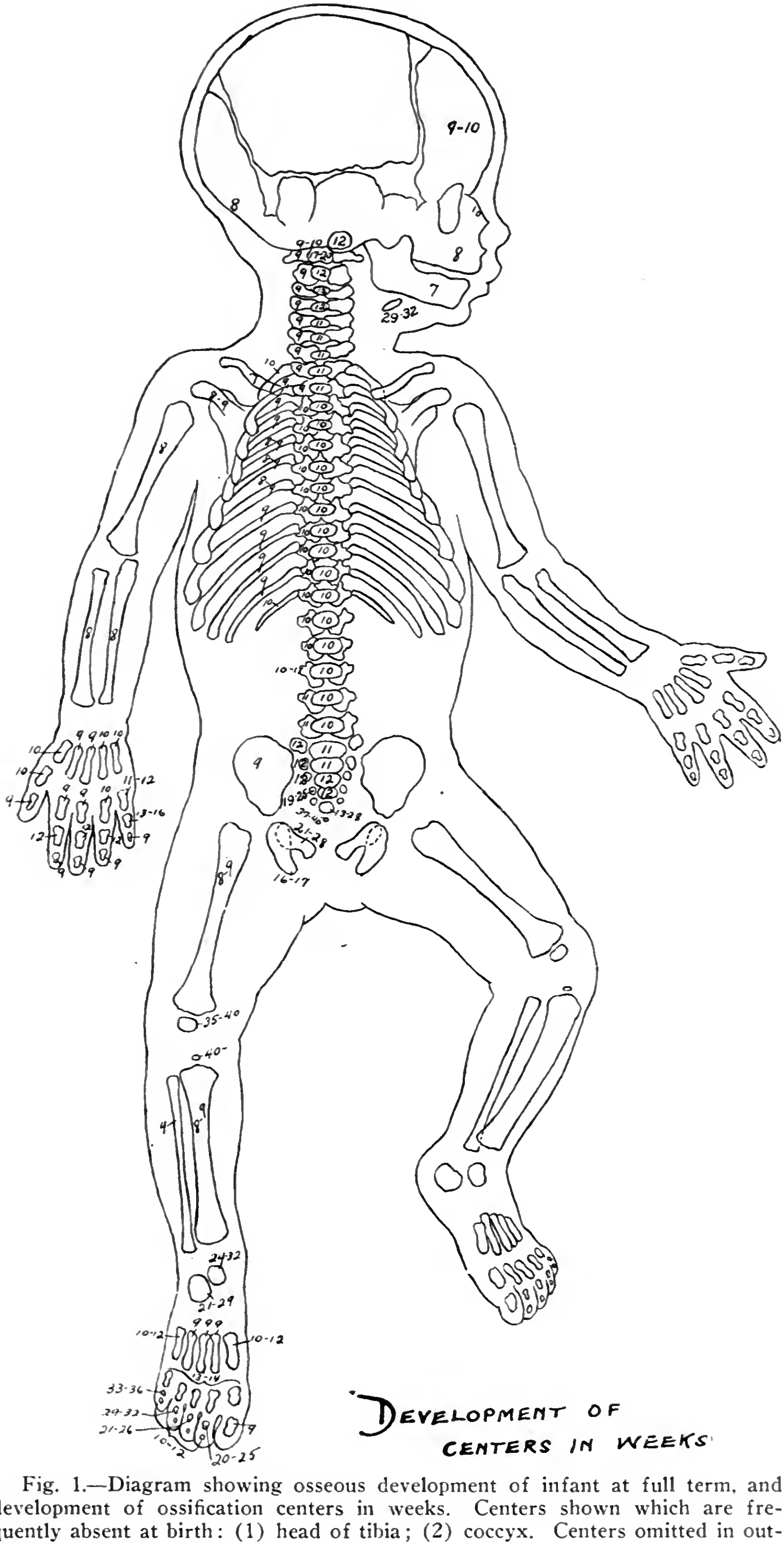

Fig. 1.—Diagram showing osseous development of infant at full term, and development of ossification centers in weeks. Centers shown which are frequently absent at birth: (1) head of tibia; (2) coccyx. Centers omitted in outline: (1) sternum; (2) hyoid.

TABLE 1.—Average Lengths in Centimeters of Normal Fetuses as Given by Different Observers

Lunar Months	Mall[8]	Von Winckel[11]	De Lee[12]	Lambertz[13]	Ahlfeld[14]	Schroeder[15]
1st*	0.25	.....	0.75-0.9			
2d	0.55- 3.0	0.9-2.5	2.5			
3d	4.1 - 9.8	7-9	7-9	6-11		
4th	11.7-18.0	10-17	10-17	11-17		
5th	19.8-25.0	18-27	17-26	17-28		
6th	26.8-31.5	28-34	28-34	26-37		
7th	33.1-37.1	35-38	35-38	35-38	36-40	
8th	38.4-42.5	40-43	43	38-42	40-43	41.2
9th	43.6-47.0	46-48	46-48	42-45	46-48	44.6
10th	48.4-50	48-50	48-50	45-52	48-50	46.0

* The length for the first two months represents the measurement from the vertex to the buttocks; all the other measurements are from vertex to sole.

TABLE 2.—Size of the Child in Centimeters. Number of Cases and Age in Days as Calculated from the Beginning of the Last Menstruation

Size	Number Cases	Age, Days
48	203	271
49	272	279
50	252	277
51	211	282
52	123	283
53	34	286
54	18	290

Fig. 2.—Photographs of fetus (exact size) : *a,* at 4 to 5 weeks; *b,* 5 to 6 weeks, and *c,* 6 to 7 weeks, respectively.

There are many physiologic and pathologic variations and numerous factors influencing the length, the weight and also other measurements of the fetus. Von Winckel[11] gives the length of the new-born as 48 to 56 cm., but children over 60 cm. have frequently been born.

Some children at term are small because of the general debility of the mother or because of acute or chronic diseases during pregnancy. Diseases of the placenta and its abnormal location usually retard the

11. Von Winckel: Handbuch der Geburtshülfe, 1903, Bergmann, Wiesbaden.

12. De Lee: The Principles and Practice of Obstetrics. Philadelphia: W. B. Saunders Co., Ed. 2, 1915.

13. Lambertz: Development of the Human Skeleton During Fetal Life. Fortschr. a. d. Geb. d. Röntgenstrahlen, Suppl. 1.

14. Ahlfeld: Von Winckel's Handbuch der Geburtshülfe, **1**, No. 1, p. 290.

15. Schroder: Quoted from von Winckel's Handbuch der Geburtshülfe.

growth of the fetus. In successive pregnancies the children at term usually increase in size.

Other Measurements of the Fetus.—Von Winckel[11] regards the circumference of the head as of importance for the diagnosis of the age of the fetus and gives the following figures:

4th month	10-14 cm.	8th month	25-30 cm.
5th month	13-18 cm.	9th month	29-33 cm.
6th month	19-24 cm.	10th month	32-37 cm.
7th month	23-28 cm.		

The weight is entirely unreliable for the estimation of the age of the fetus, because it is subject to too many variations and is much influenced by the mother's general condition, and more especially by her diet.

Thus, it is seen that even the length, which up to this time has been regarded as the most reliable criterion for the determination of the age of the fetus, has many shortcomings and allows of an error of several weeks.

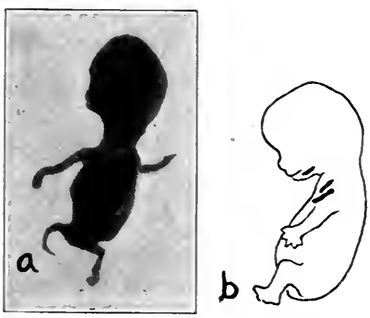

Fig. 3.—Roentgenogram (*a*) and diagram (*b*) of fetus at 7 weeks, actual size.

Roentgenograms of the Normal Development of the Skeleton.—Since roentgenograms have been found of much value in diagnosis of various diseases and conditions it was hoped that they might be of service in the diagnosis of the age of the fetus and that the development of the fetus as observed with the aid of roentgen rays might be a reliable guide for the determination of its age. The developing bones of the fetus with their centers of ossification are the only organs suitable for this purpose.

Basing our facts on the roentgenographic studies of a series of fifty-five normal cases collected during the past year and whose ages have been determined from the history of menstruation and of pregnancy and from their measurements, the normal process of development of the human skeleton as observed in roentgenograms is found to be as follows:

The ossification of the human skeleton begins in the upper part of the body and spreads very rapidly in both directions.

Seventh Week.—The first centers of ossification develop in the clavicles in the sixth to seventh week of intra-uterine life (Keibel-Mall,[8] Rauber-Kopsch,[16] but they do not become visible in the roentgenograms until in the seventh week. The ossification center appears in the middle of each clavicle and spreads rapidly in both directions.

Soon after the ossification has started in the clavicle, one center appears in each half of the mandible.

Outside of these centers of ossification usually no other centers, except occasionally that of the maxilla, are visible in roentgenograms of the 7 weeks' old fetus.

Eighth Week.—Osseous development makes rapid progress in the eighth week, and a large number of centers of ossification become visible at this time.

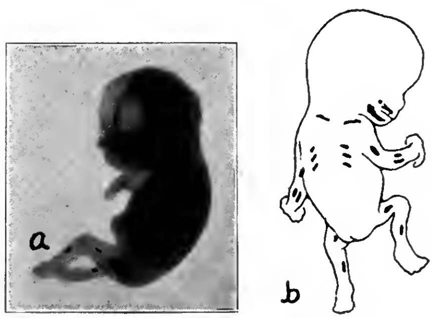

Fig. 4.—Roentgenogram (*a*) and diagram (*b*) of fetus at 8 weeks, actual size.

The following bones show centers of ossification demonstrable in roentgenograms:

Skeleton of the head: The squamous portion of the occipital bone and superior maxilla. In the latter the ossification begins soon after that of the mandible, the center appearing above the region where the alveolus of the incisor tooth is later located.

Usually no centers of ossification are present in the axial skeleton in this week.

Shoulder girdle: In the scapula a center of ossification usually appears in the eighth week, sometimes in the ninth week. The center corresponds to the position of the middle of the spine of the scapula.

Upper extremity: The humerus is the first bone of the free extrem-

16. Rauber-Kopsch: Lehrbuch der Anatomie des Menschen. Thieme, Leipsic, Ed. 10, 1914, **2.**.

ities to show a center of ossification, which appears in the diaphysis early in the eighth week. Radius and ulna follow in the order given, the centers appearing very soon after those of the humerus.

The ribs start in their ossification in the eighth week, an ossification center appearing in the region of the angle and extending slowly toward the vertebral column, but rapidly in the opposite direction. The fifth, sixth and seventh ribs, which ossify first, are visible in this period. From this region the process of ossification progresses with equal rapidity both cephalad and caudad. The last rib to ossify is usually

TABLE 3.—Time of Appearance of Centers of Ossification

HEAD	
Mandible	7th week
Occipital Bone (squamous portion)	8th week
(lateral and basilar p.)	9th-10th week
Superior maxilla	8th week
Temporal bone (petrous, mastoid and zygoma)	9th week
Sphenoid (inner lamella of pterygoid process)	9th week
(great wings)	10th week
(lesser wings)	13th week
(anterior body)	13th-14th week
Nasal bone	10th week
Frontal bone	9th-10th week
Bony labyrinth	17th-20th week
Milk teeth (rudiments)	17th-28th week
Hyoid bone (greater cornua)	29th-32d week

TABLE 4.—Time of Appearance of Centers of Ossification

SHOULDER GIRDLE	
Clavicle (diaphysis)	7th week
Scapula	8th-9th week
UPPER EXTREMITY	
Humerus (diaphysis)	8th week
Radius (diaphysis)	8th week
Ulna (diaphysis)	8th week
Phalanges, terminal	9th week
basal, 3d and 2d	9th week
basal, 4th and 1st	10th week
basal, 5th	11th-12th week
middle 3d, 4th, 2d	12th week
middle 5th	13th-16th week
Metacarpals, 2d and 3d	9th week
4th, 5th, 1st	10th-12th week

the first pair. Shortly before the first pair, the twelfth pair usually ossifies, but this is very irregular and we found it absent in several of our cases in old fetuses when other bones of the body and all the other ribs were very well developed.

Lower extremity: Centers of ossification may be occasionally seen in the diaphyses of the femur, but usually they become visible in the ninth week. The femur is the first to show a center, the tibia starting in its ossification a little later, and the fibula following very soon after the tibia.

Ninth Week.—Portions of the hand and of the foot enter the stage of ossification, these being the most important new developments in this week.

The following additional centers of ossification are visible in the head: inner lamella of the pterygoid process of sphenoid and mastoid portions of the temporal bone. The zygomatic process of the temporal bone begins to cast a shadow, its shape being somewhat pointed anteriorly and somewhat convex externally, thus resembling a needle. Bony trabeculae are often seen in the posterior root of the mastoid process. The superior maxilla forms at this time a simple triangular plate, the

TABLE 5.—Time of Appearance of Centers of Ossification

AXIAL SKELETON (VERTEBRAE)

Arches, all cervical and upper 1 or 2 dorsal	9th week
all dorsal and 1 or 2 lumbar	10th week
lower lumbar	11th week
upper sacral	12th week
4th sacral	19th-25th week
Bodies from 2d dorsal to last lumbar	10th week
from lower cervical to upper sacral	11th week
from upper cervical to lower sacral	12th week
5th sacral	13th-28th week
1st coccygeal	37th-40th week
structural arrangement	13th-16th week
odontoid process of axis	17th-20th week
Costal processes, 6th and 7th cervical	21st-33d week
5th cervical	33d-36th week
4th, 3d, 2d cervical	37th-40th week
Transverse processes, cervical and dorsal	21st-24th week
lumbar	25th-28th week

RIBS AND STERNUM

Ribs, 5th, 6th, 7th	8th-9th week
2d, 3d, 4th, 8th, 9th, 10th, 11th	9th week
1st	10th week
12th (very irregular)	10th week

STERNUM

Sternum	21st-24th week

base of which is parallel to the margin of the maxilla, the apex pointing towards the root of the nose. The malar bone may become visible towards the end of this week or during the next week.

Axial skeleton: Arches of all the cervical and upper one or two dorsal vertebrae show centers of ossification, usually no centers for bodies being visible. One center develops in each arch, the process beginning in the first cervical vertebra and proceeding caudally.

Shoulder girdle: The acromion process of the scapula begins to ossify.

Upper extremity: The terminal phalanges of all fingers begin to ossify in this week. The first beginnings of these centers are difficult to study in roentgenograms on account of their small size, but the later

stages can be easily demonstrated. Development of the centers of ossification in terminal phalanges is followed by the appearance of centers in the metacarpals which become visible in the ninth to tenth week. The following is the order of ossification in the metacarpals: second, third, fourth, fifth, first, of which the second and the third are usually visible in the ninth week.

Ribs: All the ribs, except the first and the twelfth cast shadows.

Pelvic girdle: The ilium usually appears in this week, rarely at the end of the eighth week. Ossification begins in the region of the greater sacrosciatic foramen and near the acetabulum.

Lower extremity: Centers of ossification in femur, tibia and fibula are seen. Centers begin to develop in the phalanges, the first one being

TABLE 6.—Time of Appearance of Centers of Ossification

PELVIC GIRDLE	
Ilium	9th week
Ischium (descending ramus)	16th-17th week
Os pubis (horizontal ramus)	21st-28th week
LOWER EXTREMITY	
Femur (diaphysis)	8th-9th week
(distal epiphysis)	35th-40th week
Tibia (diaphysis)	8th-9th week
(proximal epiphysis)	40th week
Fibula	9th week
Os calcis	21st-29th week
Astragalus	24th-32d week
Cuboid	40th week
Metatarsal, 2d and 3d	9th week
4th, 5th and 1st	10th-12th week
Phalanges, terminal 1st	9th week
terminal 2d, 3d, 4th	10th-12th week
terminal 5th	13th-14th week
basal 1st, 2d, 3d, 4th, 5th	13th-14th week
middle 2d	20th-25th week
middle 3d	21st-26th week
middle 4th	29th-32d week
middle 5th	33d-36th week

a center for the diaphysis of the terminal phalanx of the big toe. Diaphyses of the metatarsals follow in the same sequence and almost at the same time as corresponding portions of the hand, but with far less regularity.

Tenth Week.—Comparatively few new centers of ossification are added in this week.

Skeleton of the head: Nasal bone and frontal bone show centers of ossification. The great wing of the sphenoid becomes visible.

Axial skeleton: Bodies of the vertebrae begin to cast shadows. The process starts in the bodies of the lower dorsal vertebrae, progressing from this region with unequal rapidity in both directions. Usually the lower ten dorsal and all the lumbar vertebrae show centers of ossi-

fication in their bodies in this week. The process of ossification of the arches, progressing downward, has affected usually all the thoracic vertebrae, being more or less advanced occasionally, invading often the upper lumbar region.

Shoulder girdle: Ossification of the scapula spreads to the supraspinous fossa.

Upper extremity: Diaphyses of basal phalanges of fingers develop centers of ossification, the following being the sequence: third, second, fourth, first and fifth. Of these, usually the third, only, shows center in this week.

Ribs: At this time ossification, as a rule, is seen in all the ribs, the twelfth behaving very irregularly. It was found absent in some comparatively old fetuses far beyond the tenth week.

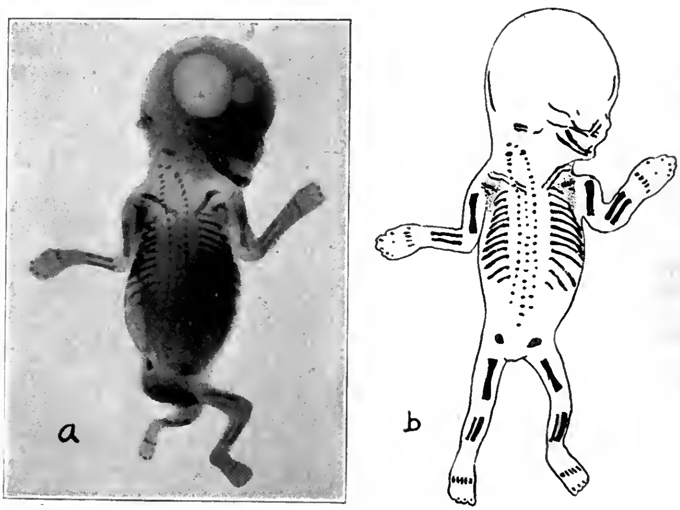

Fig. 5.—Roentgenogram (*a*) and diagram (*b*) of fetus at 10 weeks, actual size.

Lower extremity: Beginning with this week centers of ossification are present also in the terminal phalanges of the second and of the third toes.

Eleventh to Twelth Week.—In this period almost as many centers of ossification are present in the fetal skeleton as at the time of birth, so that but few are added during the period of development following the third month, and further changes in the fetal skeleton consist mostly of growth of the centers of ossification, of their fusion and of the formation of the internal structure of the bones. A fine, somewhat irregular, medullary cavity forms in the long bones, usually being seen first in the tibia.

Skeleton of the head: The tympanic ring usually becomes visible in this week, rarely at the end of the eleventh week. In pictures taken from the side, its shadow lies between the angle of the mandible and the basilar portion of the occipital bone. The median lamella of the pterygoid process reaches considerable size and is visible as a hook-shaped, curved plate with concavity posteriorly, lying behind the lower portion of the perpendicular part of the palate bone. The malar bone joins the end of the zygomatic process of the superior maxilla and that of the temporal bone. Four centers are now present in the occipital bone. The anterior sphenoidal body begins to ossify.

Axial skeleton: Ossification of the arches invades the lower lumbar region. The ossification of the bodies now appears in the lower cervical

Fig. 6.—Photograph (*a*) and roentgenogram (*b*) of transparent specimens of fetus at 10 weeks, actual size.

region and in the upper part of the sacrum, the intermediary bodies having been visible previously. There are, however, considerable variations in the time of appearance of centers of ossification in the sacral vertebrae.

Shoulder girdle: No new centers develop, the old ones increasing in size.

Upper extremity: The diaphyses of all the basal phalanges cast shadows. Middle phalanges of the third, fourth and occasionally of the second finger develop centers of ossification in their diaphyses. The middle phalanx of the fifth finger ossifies much later. Up to the end of the third month the bony diaphyses of the humerus, radius and

ulna remain longer and thicker than the corresponding bones of the lower extremity.

Pelvic girdle: Either in this period or shortly after, a third center of ossification develops in the ilium, being situated ventrally from the fused first and second centers. There is a marked irregularity in the time of appearance of the third center of the ilium, since occasionally it may appear almost three weeks after this time.

Lower extremity: The terminal phalanges of the fourth and fifth toes usually develop centers of ossification; in the fifth, however, the

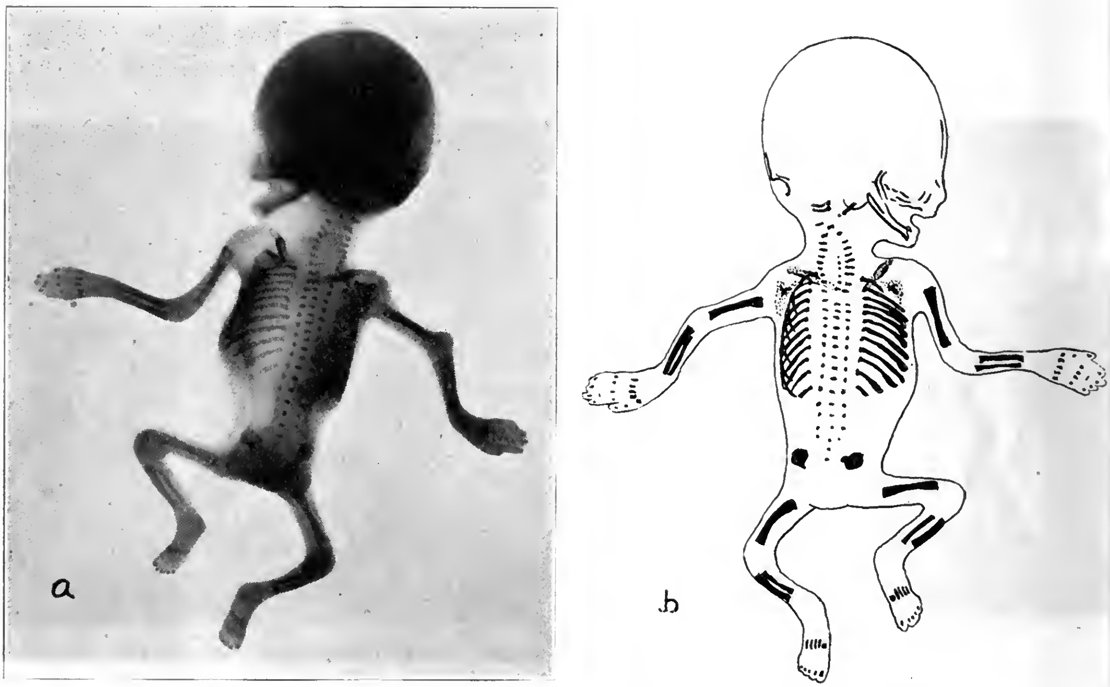

Fig. 7.—Roentgenogram (*a*) and diagram (*b*) of fetus at 11 to 12 weeks, actual size.

center may occasionally appear as late as in the thirteenth week. The bony diaphysis of the femur, which up to this time has been shorter and thinner than the bony diaphysis of the humerus, has almost reached the length of the latter, remaining, however, still somewhat thinner.

Thirteenth to Sixteenth Week.—Characteristic in the osseous development of this period is the appearance of structural arrangement in the bodies of some vertebrae and the presence of centers of ossification in the diaphyses of all of the long bones of the hand and of the foot, except the middle phalanges of toes.

Skeleton of the head: The lesser wing of the sphenoid is visible at the beginning of this period. The posterior body of the sphenoid appears about the fourteenth week.

Axial skeleton: At the end of this period all the vertebrae, with the exception of first and second lower sacral and the coccygeal, have at least one center of ossification. Arches are ossified also in the upper sacral region and the bodies from the upper cervical down to the lower sacral region. Structural arrangement becomes visible in the bodies of some vertebrae. Upper and lower plate, casting denser shadow,

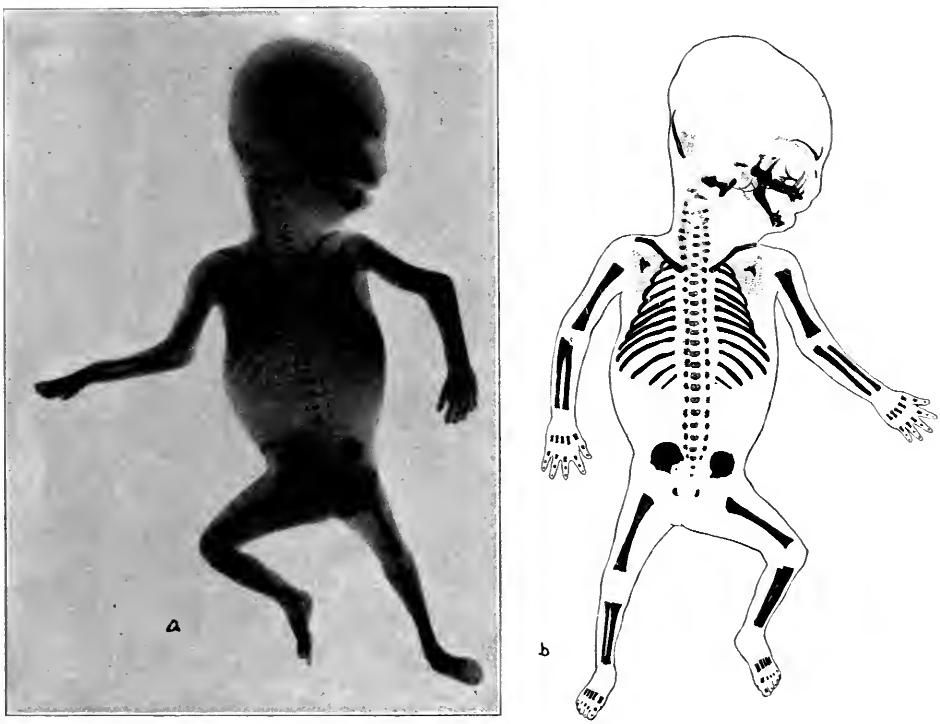

Fig. 8.—Roentgenogram (*a*) and diagram (*b*) of fetus at 13 to 16 weeks, one-half actual size.

become differentiated. A zone of lighter shadow is seen between these two plates and in the central portion of the body a flat, darker shadow appears. The greatest diameter of this darker shadow corresponds to the longitudinal axis of the fetus in lumbar and lower dorsal vertebrae; in other dorsal vertebrae it lies horizontally. These shadows appear in the bodies of the vertebrae in the region in which the primary centers made their first appearance.

Upper extremity: In the fifteenth to sixteenth week a center of ossification appears in the diaphysis of the middle phalanx of the fifth

finger, so that at this time the diaphyses of all the long bones of the hand possess centers of ossification.

Pelvic girdle: At the end of this period or somewhat later a center becomes visible in the descending ramus of the ischium. Instead of one center, two separate centers may develop in this portion of the innominate bone and they may remain separate for a long time afterwards.

Lower extremity: In the thirteenth week a center of ossification develops in the diaphysis of the terminal phalanx of the fifth toe, if it did not appear earlier. In the fourteenth week ossification in the basal phalanges begins, first in the big toe, and proceeds towards the fibular side in other toes, and up to the end of this period it usually reaches the last toe.

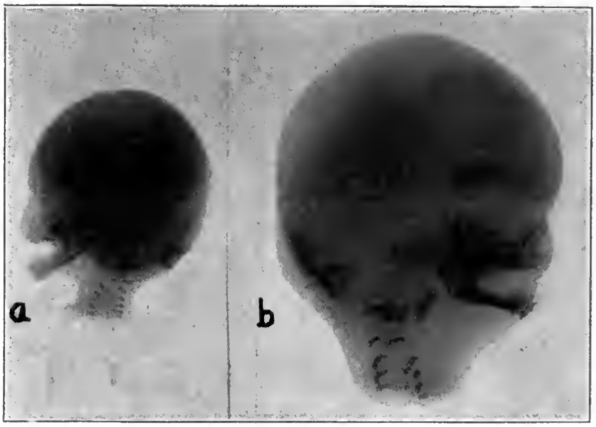

Fig. 9.—Roentgenograms of skull showing ossification centers at (*a*) 11 to 12 weeks and (*b*) 13 to 16 weeks, actual size.

Seventeenth to Twentieth Week.—In this period the bony labyrinth first appears and bone tissue begins to be formed in the rudiments of the milk teeth.

Skeleton of the head: Several new centers of ossification appear in the petrous portion of the temporal bone, but they do not show well in roentgenograms. The bony labyrinth starts in its development. In the rudiments of milk teeth, bone tissue begins to be formed and casts a shadow. The process starts in the lower incisors.

Axial skeleton: A center of ossification appears in the odontoid process of the axis. The darker shadows in the bodies of the vertebrae become more distinct and external formation and internal structure of osseous bodies of vertebrae become visible in roentgenograms. Ossi-

fication of the arches may reach the fourth sacral vertebrae at the end of this period, although this frequently occurs later.

Pelvic girdle: The twentieth week is the earliest time of appearance of a center in the horizontal ramus of the pubic bone; this, however, varies between the twentieth and the twenty-eighth week. The center is located near the margin of the obturator foramen, two centers developing occasionally.

Lower extremity: In the twentieth week a center of ossification may develop in the middle phalanx of the second toe, but this usually occurs in the twenty-first to the twenty-fourth week and frequently

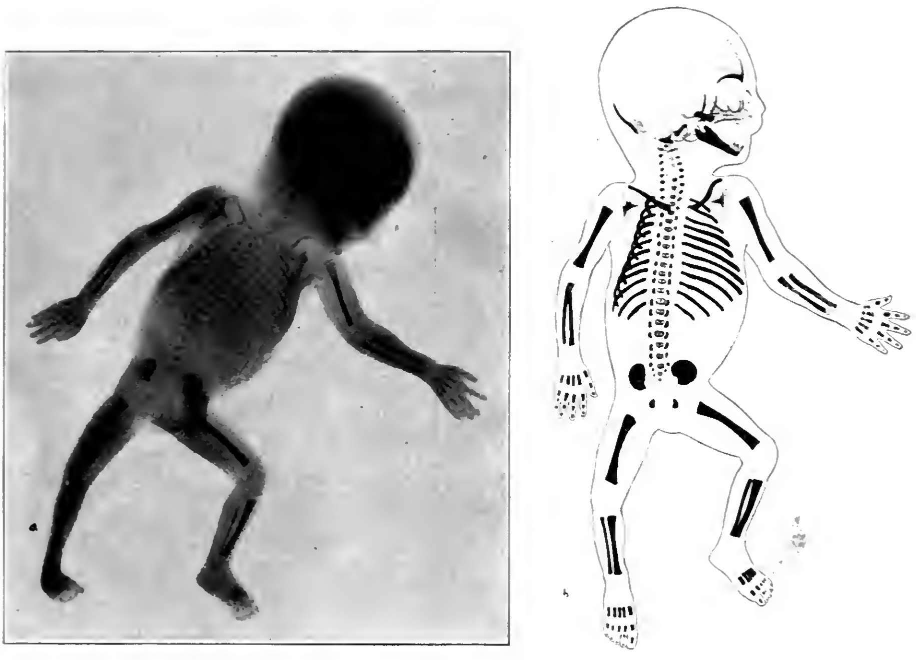

Fig. 10.—Roentgenogram (*a*) and diagram (*b*) of fetus at 17 to 20 weeks, one-third actual size.

even later than this. On the whole, there are marked differences and also individual variations in the time of appearance of centers of ossification, and also in the sequence of ossification in the phalanges of toes, especially in the basal phalanges and even more so in the middle phalanges. In the hand, however, the sequence of ossification in the phalanges is far more constant and the time of appearance of the centers is much less changeable than that of the centers in the phalanges of toes.

Twenty-First to Twenty-Fourth Week.—In this period ossification usually starts in the tarsus, os calcis being the first to show a center of

ossification. The sternum begins to develop by several centers of ossification, but there are considerable variations in the arrangement and size of these centers and also in the time of their appearance.

Skeleton of the head: The superior maxilla shows a large amount of spongiosa. Toward the twenty-fourth week the alveolar portion of the superior maxilla begins to overhang the level of the palatal plate, but develops as a real process only during the cutting of the teeth.

Axial skeleton: The costal process of the sixth cervical vertebra starts in its ossification. Shadows of transverse processes are seen in vertebrae down to the twelfth dorsal.

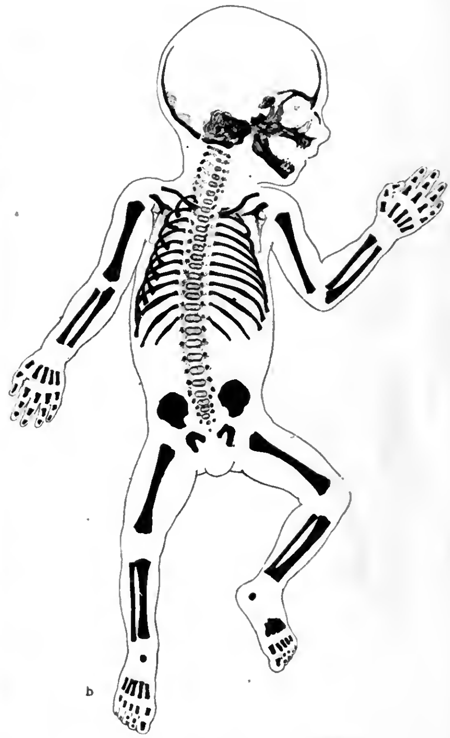

Fig. 11.—Roentgenogram (*a*) and diagram (*b*) of fetus at 25 to 28 weeks, one-fourth actual size.

Upper extremity: In this period the ossified portion of the diaphysis of the humerus reaches the articular ends and begins to overlap these so that at the distal end of the humerus both fossae (olecranon and cubital) and ulna and olecranon become visible, and later, on the proximal end of the humerus an indication of the medial and posterior portion of the neck appears.

The sternum starts in its ossification. Usually one center forms in the manubrium first and this is followed soon afterward by several

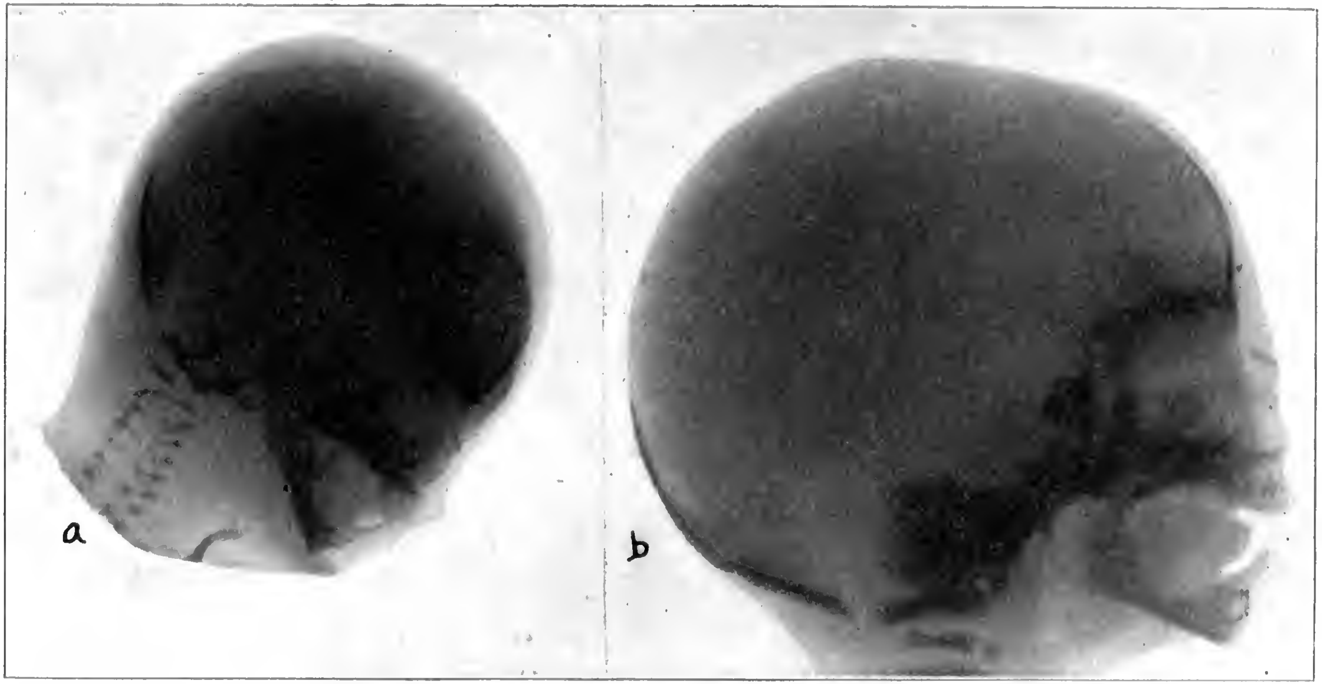

Fig. 12.—Roentgenograms of skull of fetus showing ossification centers at (*a*) 17 to 20 weeks and (*b*) 25 to 28 weeks, actual size.

centers in the body of the sternum. The centers form a longitudinal row first, and soon they assume a round or elliptical form. Not seldom the first centers of ossification appear in the upper part of the body between the second and the third costal cartilages. The position of the ossification centers of the sternum corresponds usually to the level of the intercostal spaces.

Lower extremity: A center of ossification develops in os calcis, its appearance being occasionally delayed by from four to eight weeks.

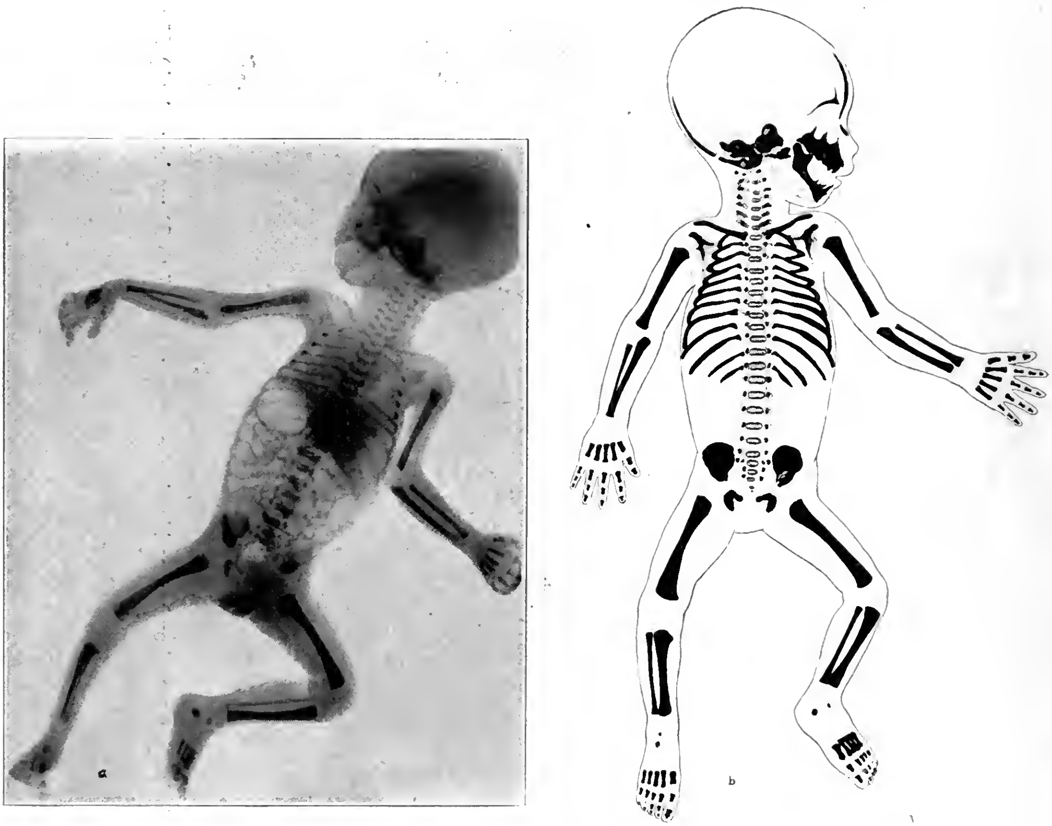

Fig. 13.—Roentgenogram (*a*) and diagram (*b*) of fetus at 29 to 32 weeks, one-fourth actual size.

Sometimes it is followed by the appearance of a center in the astragalus. The middle phalanx of the second toe, and occasionally that of the third toe, acquire a center of ossification in their diaphyses.

Twenty-Fifth to Twenty-Eighth Week.—The rudiments of all the milk teeth have entered the stage of ossification in this month.

The development of the transverse processes of the vertebrae progresses down to the last lumbar vertebra. At the end of this period a

center of ossification may develop in the lateral masses of the first and of the second sacral vertebrae. The body of the fifth and the arches of the fourth sacral vertebrae become ossified at this time, rarely earlier.

A center of ossification develops in the astragalus.

In the horizontal ramus of the pubic bone the center may develop as late as in this period.

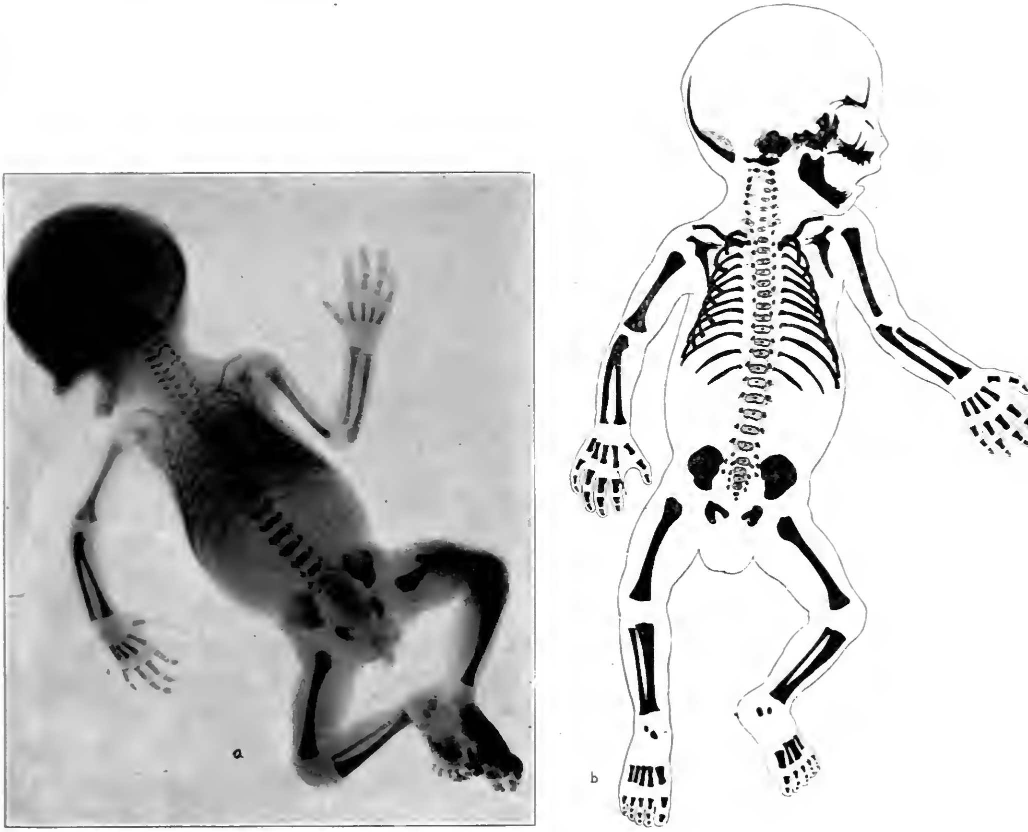

Fig. 14.—Roentgenogram (*a*) and diagram (*b*) of fetus at 33 to 36 weeks, one-fourth actual size.

Twenty-Ninth to Thirty-Second Week.—The greater cornua of the hyoid bone usually become visible, appearing as cone-shaped processes directed obliquely upwards at the level of the second cervical vertebra.

The lateral masses of the first and second sacral vertebrae ossify usually at this time.

In the sternum three or more large centers of ossification are visible.

The middle phalanx of the fourth toe frequently starts in its ossification during the period.

Thirty-Third to Thirty-Sixth Week.—This period is the earliest time at which the first epiphyseal center may appear, that of the distal epiphysis of the femur. Usually, however, this center appears later, at about the time of birth.

The costal process of the sixth and of the fifth cervical vertebrae start in their ossification.

Thirty-Seventh to Fortieth Week.—The middle turbinates ossify at the end of the fetal period and shortly before birth the rudiments of the first permanent molar teeth begin to ossify.

The costal process begins to ossify in the fourth, the third and the second cervical vertebrae; the first coccygeal vertebra usually ossifies during the last weeks before birth and vertical arrangement of trabeculae becomes visible in the bodies of the vertebrae.

A center of ossification appears in the proximal epiphysis of the tibia just before birth in a majority of cases, and ossification in the cuboid frequently starts before birth, usually by several centers, although in some cases it may not be visible even in the new-born.

The New-Born.—A center of ossification in the distal epiphysis of the femur is so frequent in the new-born that Lambertz[13] calls it a sign of maturity. This is frequently the only epiphyseal center present in the new-born. Poirier[17] gives a summary of the literature on the time of the appearance of the epiphysis at the distal end of the femur. Schwegel found it to appear between birth and the third year. Casper in the ninth fetal month. Hartmann found it lacking in 12 per cent. of cases at birth and in 7 per cent. of cases present as early as the eighth fetal month.

The four parts of the occipital bone (basilar, two lateral and the squamous) are separated from each other by thin layers of cartilage. The mastoid portion of the temporal bone is not ossified in its entire extent, a serrated line marking the boundary between bony and cartilaginous portions of the mastoid part. The lateral halves of the frontal bone are separated. The body of the hyoid bone is usually ossified. Both halves of the mandible, as a rule, are united by connective tissue.

The vertebrae are ossified in all their essential parts, including transverse and articular processes of the arches, but the centers of ossification are separated from each other by cartilage. The first coccygeal vertebra is usually ossified by this time.

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17. Poirier: Traite d'anatomie, **1,** 227.

Fig. 15.—Roentgenograms of skull of fetus showing ossification centers at (*a*) 29 to 32 weeks and (*b*) 33 to 36 weeks, actual size.

In some cases the proximal epiphysis of the humerus is ossified. In the hand all bones are ossified except the carpus, in which centers of ossification in os magnum and unciform may be seen only very rarely.

At birth the ossified portion of the os pubis surrounds usually a portion of the anterior boundary of the obturator foramen, but the region of the symphysis and upper margin of the horizontal ramus of os pubis remain cartilaginous. The following portions of the innominate bone are not ossified in the new-born: the crest of the ilium with superior spines, acetabulum, spine of ischium and ascending ramus of ischium.

The middle phalanx of the fourth toe is frequently, that of the fifth toe always, cartilaginous in the new-born; in the fourth toe, however, the middle phalanx may start in its ossification in the eighth fetal month. The following portions of the leg are usually not ossified in the new-born: proximal epiphysis of tibia and of the fibula, epiphyses of metatarsal bones and of phalanges, the cuboid and the three cuneiform bones.

OTHER METHODS OF STUDYING OSSEOUS DEVELOPMENT COMPARED

We have compared the process of ossification, as observed in the roentgenograms of the fetuses studied with the roentgenographic studies of Alexander,[18] Bade,[19] Hasselwander[20] and Lambertz,[13] and found that the time of appearance of centers of ossification pretty well agrees, in general, there being minor differences only.

Compared with the studies of Mall, who used transparent specimens of embryos and fetuses for observing the appearance of centers of ossification, we find that by using transparent specimens he was able to demonstrate the minute centers of ossification generally about one week earlier than they are demonstrable by roentgenograms. This observation also agrees with textbooks of anatomy (Rauber-Kopsch, Gray[21]) which have been consulted for this purpose, and it is found that they place the time of appearance of various centers about one week ahead of the time at which the centers cast shadows in roentgenograms large enough to be visible.

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18. Alexander: The Development of the Osseous Vertebral Column. Fortschr. a. d. Geb. d. Röntgenstrahlen, Suppl. 13.

19. Bade: Short Description of Ten Roentgenologically Examined Fetuses. Centralbl. f. Gynäk., 1899, p. 1031.

20. Hasselwander: Studies of Ossification of the Skeleton of the Human Foot. Ztschr. f. Morphol. u. Anthropol., 1903, **5,** 438.

21. Gray-Spitzka: Anatomy Descriptive and Applied. Ed. 18. Lea & Febiger, Philadelphia and New York, 1910.

By courtesy of Dr. Roy Lee Moodie of the Department of Anatomy of the University of Illinois we obtained transparent specimens of a pair of twins from his embryologic collection and made roentgenograms of them. By studying these roentgenograms and specimens we found the following differences:

	Roentgenograms	Transparent Specimens
Basal phalanges of fingers	3d	2d, 3d, 4th
Terminal phalanges of toes	1st, 2d 3d	1st, 2d, 3d, 4th
Bodies of vertebrae	9 lower dorsal	9 to 10 lower dorsal, respectively
	All lumbar	All lumbar
	1st sacral	1st, 2d sacral
Arches of vertebrae	Upper 3 lumbar	Upper 3 to all lumbar, respectively

Thus the transparent specimens show in the tenth week centers that become visible in the roentgenogram only in the eleventh to twelfth week.

VARIATIONS IN OSSECUS DEVELOPMENT

There are, as might be expected, some variations in the normal process of ossification, and it is also influenced by pathologic conditions of the mother and of the fetus (for example, syphilis, rickets, osteogenesis imperfecta, etc.). In general, these pathologic processes may well be diagnosed in the roentgenograms so that an error may easily be prevented. In some portions of the skeleton the ossification is less regular than in others, and as a general rule the more caudad the portions of the skeleton are, the more they are subject to variations in the process of ossification; and the centers which develop at a later period of fetal life are also more variable. Thus, there are considerable variations in the time of appearance of centers of ossification in the sacral vertebrae. The foot, as a general rule, is unreliable as an indicator of the age of the fetus. The ossification of the sternum is also irregular in the time of appearance, size and arrangement of the centers of ossification. The twelfth rib is also very irregular, and we found it absent in roentgenograms of the fetus from the thirteenth to sixteenth week, and also in some other older ones, although, as a rule, the twelfth rib appears in the tenth or in the eleventh week. Some of the centers, although demonstrable by careful examination, are so small as to be easily overlooked, and this may lead to an error. For this reason it is necessary to know what centers we may expect at that particular age of the fetus, and we should look for them in good light with a magnifying glass.

Bade[19] has examined roentgenograms of twin fetuses, one of which was 5.8 cm. long, weighing 8 gm., and the other 6.3 cm. long, weighing 11 gm. The only difference in the stage of ossification was that the

larger fetus showed two more centers in the arches of the vertebrae and two additional centers in terminal phalanges of the fingers.

In a fetus 7.1 cm. long and weighing 25 gm., the same author found, however, that the ossification did not progress as far as in the above mentioned twins, which were shorter. This delay in ossification was in the ribs (the last one not being visible, although all visible in the twins), while the axial skeleton showed only 5 bodies and 21 arches, as compared with 18 bodies and 22 and 24 arches, respectively, in the twins.

Alexander[18] found that while the ossification has been normal in other parts of the body, it has been occasionally delayed in the vertebral column.

He observed also twin fetuses measuring 8.9 cm. and 9.1 cm. in length, respectively. The only difference in ossification in these two fetuses was that in the larger one there was an ossification center in the third sacral vertebra, while in the shorter one the second sacral vertebra was the last one containing a demonstrable center.

In the twins from Dr. Moodie's collection which we have studied, the only differences in the stage of ossification are in the axial skeleton, one fetus showing centers for seventeen bodies and twenty-four arches on each side and the other only fifteen bodies and twenty-two arches on each side.

But in spite of these variations, the process of ossification seems to be more constant for a particular age than the length of the fetus. Mall,[22] in his article on ossification in embryos up to 100 days old, concludes that "the remarkable regularity of the appearance of the bones makes of them the best index of the size and of the age of embryo we now possess."

LIMITATIONS OF ACCURACY

In the first half of pregnancy the estimation of the age of the fetus may be made with greater accuracy because many more new centers appear in the first months, and also because the time of appearance of the earlier centers is more constant. In later months centers of the lower part of the skeleton mostly are available for study, and these are less constant in the time of their appearance. We have intentionally made our groupings broad enough to cover minor errors in diagnosis, but more careful subsequent studies may refine the diagnosis to such a degree that determination of age will be possible within the period of one week in the first half of the pregnancy, and within two weeks in the second half of the pregnancy.

22. Mall: On Ossification Centers in Human Embryos Less Than One Hundred Days Old. Am. Jour. Anat., 1906, **5**, 433.

DIFFERENT VALUES OF THE DIFFERENT PORTIONS OF THE BODY

In the very early period (second month) the stage of ossification of clavicle and mandible is of chief importance, and on the basis of presence or absence of these centers determination of the age is made. Both roentgenograms and transparent specimens show that the time of appearance of these centers is almost constant, which makes them of cardinal value in diagnosis.

Next in importance are the centers of the upper extremity, and especially of the hand (metacarpals and phalanges) which are very regular, not only in the time of their appearance, but also in their sequence. The ossification of the diaphysis of the long bones of the arms extends from the eighth to the sixteenth week, and during this period the determination of the age may frequently be made from a good roentgenogram of the hand alone.

The progress of ossification of the head is also of considerable diagnostic importance, but the centers in many bones of the head are very difficult of demonstration. Those, however, that can be well demonstrated are of much value in the determination of the age. This is especially true of the occipital bone, superior maxilla, tympanic ring, nasal bone and hyoid bone.

The axial skeleton (the vertebral column) is less reliable than the foregoing named portions of the skeleton, and especially its lower portion is of little value in diagnosis of age. It is not the absolute number of arches or of the bodies ossified which decides the diagnosis as to the age of the fetus, but more the region involved and the extent of the development in the particular region of the vertebral column (cervical, dorsal, lumbar, sacral). On the other hand, however, the facts that the process of ossification of the vertebral column extends from the ninth week throughout the life of the fetus, and all its centers, as a rule, are well demonstrable, make it of especial value for at least approximate determination, although it must not be forgotten that occasionally the process of ossification may be delayed in the vertebral column, while it is normal and regular in other portions of the body.

The sternum is unreliable as an index of age and its centers are frequently difficult to demonstrate. The ribs are fairly constant, except the twelfth pair, which, as previously mentioned, may not show at all in roentgenograms of comparatively old fetuses.

While the ossifications of the long bones of the legs are pretty regular, since they appear at an early period, ossification in the foot is very irregular and the stage of ossification of the foot is of little

value in the determination of the age of the fetus. The osseous development of the foot extends from the ninth week to the end of the fetal period (not being, however, completed even at this time) and during this time there are very marked variations, especially in the centers which appear late in the fetal period.

From the above it may be seen that, as a general rule, the earlier a center appears the more regular it is, and since the process of ossification starts in the cephalic region and spreads caudally, it is also true that the more caudad a skeletal segment is situated the more it is subject to variations and irregularities.

ADVANTAGES OF THE ROENTGENOGRAPHIC METHOD

The peculiar advantage of the roentgenographic method for determining the age of the fetus lies in the fact that while in the determination of age according to the length we base our final conclusion usually on one, rarely on two or three measurements expressing different lengths of the fetus, in the roentgenographic method many centers of ossification are the factors taken into consideration before arriving at a final conclusion; and they act as check on each other and quite frequently the roentgenograms alone give us information as to whether the fetus is normal or not, a point which seldom may be determined from measurements alone.

TECHNIC

In studying the roentgenograms it is well to use a reading glass of about 4 inches in diameter, since some centers of ossification may be so small as to be very easily overlooked when sought for with the naked eye.

If only one exposure of the fetus is made, then the best position to show as many ossification centers as possible is as follows: The back lying flat on the plate, head turned completely to one side so that the side of the head lies on the plate and lateral exposure is obtained. (It should be remembered in the study of the skull that both halves of the skull are usually visible.) Arms and fingers should be extended and fingers spread as far as possible from one another. One hand should be pronated and the other supinated, the lateral exposure, which is often of so much value in roentgenograms taken for the purpose of surgical diagnosis, not being of much value, since in this position shadows of phalanges of fingers and of metacarpals are superimposed and cannot be well differentiated. The legs should also be extended and feet put into such a position that all metatarsals and phalanges are shown.

CONCLUSIONS

1. The stage of ossification of the skeleton of the fetus as observed in roentgenograms is of considerable practical importance in determining the age of the fetus.

2. The roentgenographic method of determining the age of the fetus is more reliable than determination of age based on length and other measurements, since osseous development is more regular and offers many more factors for consideration; one part of the body is a criterion of normality for the other parts, and pathology may often be readily recognized.

3. In the early months more accurate determination is possible than in the later months, and the roentgenographic method is undoubtedly capable of much greater refinement by further studies and observations.

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INTERNAL HYDROCEPHALUS

SECOND PAPER *

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In a recent communication a series of cases of internal hydrocephalus was presented and subdivided into two apparently distinct anatomic varieties — obstructive hydrocephalus and communicating hydrocephalus. These two groups were sharply differentiated by an anatomic difference, demonstrated by the introduction of a neutral solution of phenolsulphonephthalein into the cerebral ventricles and almost immediately testing for its presence in the spinal fluid. In the obstructive type, this solution introduced into the ventricles failed to appear in the spinal fluid; in the communicating type it appeared promptly in the spinal fluid.

Clinically, the two varieties appeared identical, and it was only by this test that hydrocephalus could be subdivided. The growth of the head seemed about equally rapid, the etiology was equally obscure, and either variety might be congenital or acquired.

By an estimation of the amount of phenolsulphonephthalein excreted by the kidneys following the intraventricular and intraspinal introduction, a quantitative absorption of cerebrospinal fluid could be estimated in each type of hydrocephalus and a second very important physiologic difference was demonstrated. In the obstructive type of hydrocephalus the absorption, which is restricted to the cerebral ventricles, is practically nil — less than 1 per cent., as contrasted with a normal of 12 to 20 per cent. (Fig. 2). In the communicating type, the absorption is 2 to 5 per cent., as contrasted with the same normal (Fig. 1). The similarity of the two groups is that in both there is a tremendous diminution in the absorption of cerebrospinal fluid. This is the reason hydrocephalus develops in both the obstructive and communicating types of hydrocephalus; that is, diminished absorption of cerebrospinal fluid with an unaffected production.

It was also shown by a series of experiments that cerebrospinal fluid is produced in the ventricles and is absorbed in the subarachnoid

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space, and that the blood vessels of the entire spinal and cranial subarachnoid space participate in the absorption. It was further shown that in the obstructive type of hydrocephalus, the absorption of cerebrospinal fluid from the spinal subarachnoid space was normal. Hydrocephalus then resulted because a mechanical obstruction prevented the cerebrospinal fluid from leaving the ventricles of the brain, where there is no absorption, to the subarachnoid space, where the absorption may be normal.

In the communicating type of hydrocephalus there was a great diminution in the absorption of cerebrospinal fluid from the subarachnoid space. Although the cerebrospinal fluid passed freely from the ventricles, hydrocephalus resulted because an adequate absorption did not occur from the subarachnoid space.

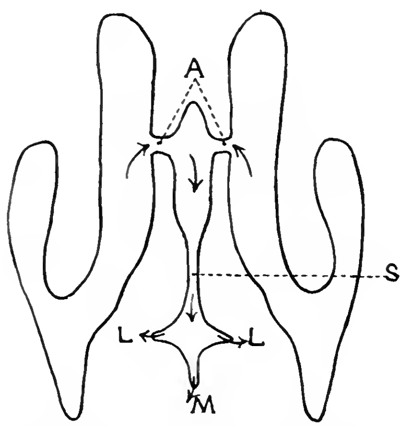

Fig. 1.—Diagram of the cerebral ventricular system, showing the intracerebral course of the cerebrospinal fluid. The three arrows at the base (*L, L,* and *M*) show the only three points of exit from the entire ventricular system. A block at *A* would produce a unilateral hydrocephalus involving only one ventricle; a block at *S* would produce an internal hydrocephalus involving both lateral ventricles; and to obtain a complete obstruction at the base, the two foramina of Luschka and the foramen of Magendie (*L, L,* and *M*) would have to be occluded.

A = foramen of Monroe; *S* = aqueduct of Sylvius; *L, L* = foramina of Luschka; *M* = foramen of Magendie.

From a physiologic standpoint, therefore, both varieties of hydrocephalus result from the same cause — a diminished absorption. Although there is an anatomic difference in the patency or closure of the foramina of exit from the ventricles, the absorption is only slightly greater where the foramina are open.

In the previous communication a series of cases of obstructive hydrocephalus was shown in which the pathologic findings verified the clinical evidence of an existing obstruction to the outflow of cere-

TABLE 1.—Cases of Communicating Hydrocephalus Studied with Phenolsulphonephthalein Test

Cases	Age	Absorption After Ventricular Injection		Absorption After Subarachnoid (Spinal) Injection		Communication, Ventricles and Subarachnoid Space; Appearance in Spinal Canal; Ventricular Injection, Min.	History	Postmortem Findings
		Time of Appearance, Minutes	Two-Hour Absorption, per Cent.	Time of Appearance, Minutes	Two-Hour Absorption, per Cent.			
1. R. G.	18 months	30	2.0	..	11.0	1	Definite history of meningitis at 7 months; hydrocephalus followed immediately	Living
		20	2.3	13	7.0	2		
2. M. R.	11 mos. (during meningitis)	13-15	6.5	..	....	7	Meningitis followed by hydrocephalus, which healed spontaneously	Living (spontaneous recovery)
	(during hydrocephalus)	20	0.5	8	14.0-9.5	2		
	9 months later	..	...	8	15.0			
	3 years later	..	...	..	60.0			
3. H. N.	8 months	25	4.4	..	10.0	20	Hydrocephalus noted 6 weeks after birth; acute illness 3 days after birth; meningitis (?)	Living
		25	4.0	..	10.0	13		
4. J. C.	16 months	30	4.0	..	....	1	....	None
5. W. F.	6 months	..	4.5	..	16.0	3	Congenital..................	Living
6. W. F.	4 months	..	3.0	..	....	2	Convulsion and fever three days after birth	Living
7. E. W.	3 months	..	3.0	..	8.5	1	Meningitis (meningococcus)	None
8. P. G.	8 months	..	5.0	..	10.0	Less than 7 min.	....	None
9. F. C.	4 months	..	2.0	..	....	7	Meningocele.................	Adhesions at base
10. H. B.	4 months	..	...	..	....	5	Meningocele.................	Adhesions at base
11. F. W.	6 months	16	2.0	12	10.0	Slight in less than 4½ hours. None in an observation several weeks later	Meningocele; large head at birth	Adhesions at base
		25	1.0	..	....			

brospinal fluid from the ventricles. Since then, numerous other cases have been studied, in all of which an obstruction was invariably found when the phenolsulphonephthalein test indicated such an obstruction during life. It is needless to present these cases in detail, as they merely confirm the previous observations, differing only in the details of the character and location of the obstruction. The accompanying tabulation of these cases (Table 2) gives in condensed form all the fundamental facts concerning the added group of cases of hydrocephalus with obstruction.

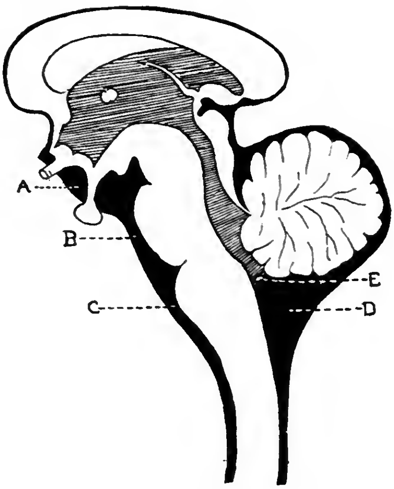

Fig. 2.—Diagram representing the midsagittal view of the brain stem, showing the ventricular system (in cross lines) and the subarachnoid system (in black). The communication between the two systems is at *E* (foramen of Magendie). The foramina of Luschka are not shown.

A = cisterna interpeduncularis; *B* = cisterna pontis; *C, D* = cisterna cerebellomedullaris (cisterna magna).

Although a small series of cases of communicating hydrocephalus was studied by the foregoing mentioned methods and presented in the earlier paper, we were unable to obtain any pathologic examinations to explain the clinical findings, and final conclusions on the etiology of this form of hydrocephalus were necessarily deferred, although the conclusions suggested from the tests strikingly anticipated the subsequent pathologic findings. It is largely the purpose of this communication to fill this pathologic deficiency and give the findings at necropsy of four cases of communicating hydrocephalus and to present the pathologic findings which result in the production of this so-called idiopathic disease. All the cases studied are from the services of Professor Halsted and Professor Howland, and it is due to their privileges and continued interest that this contribution is made possible.

I. COMMUNICATING INTERNAL HYDROCEPHALUS

(*a*). *Demonstration of the Communication.*—Eleven cases of communicating hydrocephalus have been studied. In each of these the communication has been demonstrated by the phenolsulphonephthalein test. This is the only absolute method of differentiation of the two

TABLE 2.—Cases of Internal Hydrocephalus with Obstruction,—

Cases	Age	Absorption After Ventricular Introduction		Absorption After Spinal Introduction		Communication Ventricle and Subarachnoid Space; Time of Appearance
		Time of Appearance, Minutes	Two-Hour Absorption, per Cent.	Time of Appearance, Minutes	Two-Hour Absorption, per Cent.	
1. P. G.	7 months	45	0.75	6	62	None in 45 min.
2. A. H.	6 months	40	1.0	..	..	None in 2 hours
3. N. P.	6 weeks	45	1.0	..	..	None in 20 min.
4. N. M.	2 years	40	0.50	6	35	None in 2 days
		35	0.50			
5. M. R.	13 months	40	0.50	8	25	None in 1⅓ hrs.
		20	0.9			
6. F. W.	6 months	16	2.0	12	10	Trace in less than 4½ hrs.
		25	1.0			None in 2d observation in 3 hours
7. M. N.	5 months	30	1.5	..	35	None in 30 min. Faint trace in 14 hours
8. R. C.	2 months	..	1.2	..	30	None in 2 hours
9. R. S.	6 weeks	..	2.0	..	..	None in 2 hours
10. L. S.	19 months	..	1.5	..	56	None in 2 hours
11. J. S.	8 months	..	0.5	..	35	None in 2 hours
12. J. B.	3 months	..	0.5	..	..	None in 40 min.
13. A. C.	16 months	..	0.5	..	..	None in 1 hour
14. J. M.	2½ years	..	2.0	..	..	None in 1 hour
15. J. F.	5 years	..	0.5	..	45 41	None in 1 hour

types of hydrocephalus. One can often tell from the amount of fluid obtained by lumbar puncture whether a communication exists, but more frequently this is misleading. If only 3 or 4 c.c. are obtainable on more than one occasion, it is fairly safe to assume that the obstruc-

tion is complete and exists at the foramina of Luschke and Magendie, because all the fluid formed from the choroid plexus is retained in the ventricles. On the other hand, if an obstruction exists at the aqueduct of Sylvius, a large amount of fluid can be obtained by lumbar puncture because the choroid plexus of the fourth ventricle, including

—Studied with the Phenolsulphonephthalein Test

Duration of Excretion		History	Postmortem Findings
Ventricle	Spinal Canal		
8% excreted in 12 hours; three days later, concentration of phenolsulphonephthalein in the urine was diminished	Less than 12 hours	Tuberculous meningitis; meningocele since birth	Exudate over base of brain occluding the foramina of exit
....	....	Congenital: myelomeningocele also present	Occlusion of aqueduct of Sylvius
....	....	Congenital...............	Total absence of aqueduct of Sylvius
11 days; 6.1 % first 24 hours; 7.5% second 24 hours; 5.7% third 24 hours	21 hours	Congenital...............	Died at age of 5 years. Double obstruction: one at aqueduct, the other at foramina of Magendie and Luschka
....	....	Meningitis at 4 months; previously normal	Absence of foramina of Luschka and Magendie. Fourth ventricle a large cyst. Marked thickening of pia-arachnoid
7 days	48 hours	Congenital; syringomyelocele; no history of meningitis	Chronic inflammatory process; adhesions at base occluding foramina of exit
....	....	Congenital...............	Living
....	....	Congenital...............	Obstruction at foramina of Magendie and Luschka; enormous fourth ventricle, like a huge cyst
....	....	Congenital...............	No necropsy
....	....	Meningitis lasting one month when 1 year old	Living
....	....	Meningitis; congenital....	Very dense adhesions at base of brain, disclosed at operation; child still living
....	....	Congenital...............	No necropsy
....	....	Acute meningitis..........	Thick exudate of acute meningitis at base of brain
....	....	Acute meningitis..........	Living
....	....	Tumor....................	Glioma in midbrain occluding aqueduct of Sylvius

the flocculi, is still producing fluid which passes freely into the subarachnoid space. It must be remembered that even in the highest grades of hydrocephalus it is impossible to withdraw more than a certain amount of fluid by needle, either from the ventricle or the sub-

arachnoid space, because a balance between intracranial and extracranial pressure is reached before the ventricles are emptied, and air cannot enter the needle to displace more fluid. False interpretations can be avoided and the existence of communication or obstruction determined with accuracy by the phenolsulphonephthalein test. It should be emphasized again that the ordinary solution of phenolsulphonephthalein is strongly alkaline and produces a marked reaction. A neutral solution which can be used with a minimum degree of danger has been prepared for us by Hynson, Westcott & Dunning. The solution should be freshly prepared.

Phenolsulphonephthalein appears in the spinal fluid in one to three minutes after its introduction into the ventricles where hydrocephalus does not exist. Almost the same obtains in communicating hydrocephalus, although the time in many cases is five to seven minutes, and in one instance was twenty minutes. This increased period was reduced to thirteen minutes by the upright position.

The increased amount of cerebrospinal fluid present in hydrocephalus seems to cause no appreciable delay in the transmission of the dye from the ventricles to the spinal canal. Why the delay should be so much greater in the single instance is not entirely clear, although adhesions along the spinal cord suggest a possible explanation. In cases in which adhesions are present at the base of the brain, the same condition frequently exists along the entire spinal canal, and it is natural to assume that these may delay the descent of the dye.

One patient showed a trace of phenolsulphonephthalein when a lumbar puncture was made four and a half hours after the ventricular introduction, although it was absent one-half hour after its introduction. Several weeks later a similar test was performed and there was a complete obstruction. We must assume a very trivial communication to have existed in this case, and later to have been closed over. At necropsy very dense adhesions totally occluded the foramina of exit from the fourth ventricle. No doubt this cordon of adhesions was becoming progressively tighter and the first phenolsulphonephthalein test caught the condition in the terminal stages of the transition from a communicating hydrocephalus to an obstructive hydrocephalus.

(*b*). *Quantitative Absorption in Communicating Internal Hydrocephalus.*—There is very little to add to our previous report on the quantitative absorption of cerebrospinal fluid except the confirmation of additional material. The variation of the amount of absorption is within narrow limits; the average is 3 to 4 per cent. during a two-hour period, the highest 5 per cent., and the lowest 0.5 per cent. The absorption following introduction into the normal ventricle is 12 to 20 per cent. When introduced into the spinal canal the variation is

also small. The average two-hour absorption is 10 per cent., the highest 16 per cent., the lowest 7 per cent., the normal 35 to 60 per cent. The time of first appearance in the urine is also greatly delayed following either intraventricular or intraspinal injection.

One interesting case has been under observation for four years. The child was first seen with an acute epidemic cerebrospinal meningitis, and the absorption tests showed a moderate delay and diminution in absorption following the ventricular test. The ventricles were shown to communicate with the subarachnoid space. A few weeks later, after the subsidence of the acute meningitis, the child was again brought to the hospital apparently becoming blind and having an

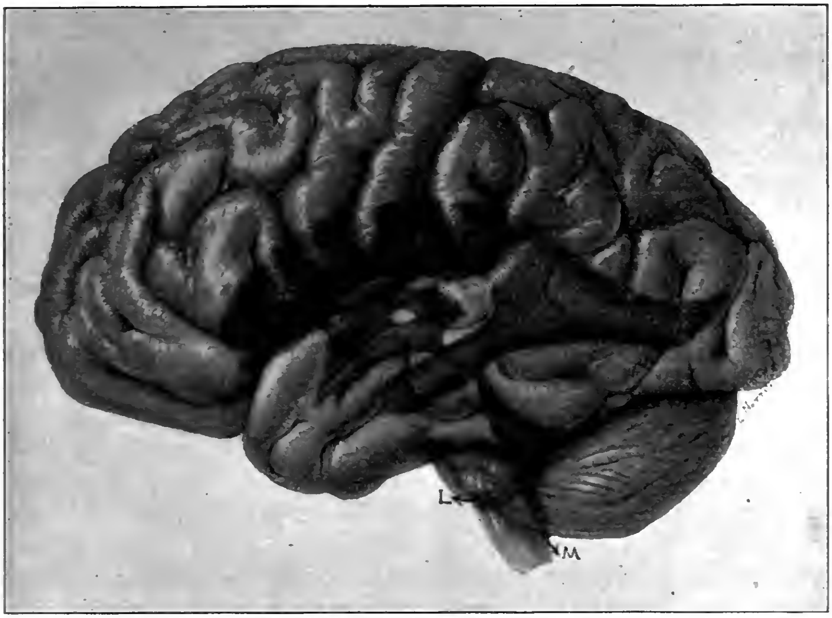

Fig. 3.—Plastic representation of a lateral view of the ventricular system, to show the relation of the structures of the brain (modified from Gray's Anatomy). L = foramen of Luschka; M = foramen of Magendie.

enlarged head, with a bulging tense anterior fontanel. Large amounts of cerebrospinal fluid were obtainable both from the ventricles and the subarachnoid space. The condition was obviously internal hydrocephalus, which was shown to be of the communicating variety. The absorption from the ventricles (0.5 per cent.) and subarachnoid space (14 and 9.5 per cent. on two occasions) was characteristically low. Phenolsulphonephthalein appeared in the spinal canal two minutes after its introduction into the ventricles. The condition seemed hopeless, and the parents were so instructed. Much to our surprise, four

years later the patient again appeared, with a fractured skull, but the hydrocephalus had apparently cleared, and the child on discharge appeared entirely normal. Tests at this time showed 50 per cent., or a normal phenolsulphonephthalein output from the subarachnoid space. The roentgenogram of the skull was negative.

(*c*). *Pathological Findings in Communicating Internal Hydrocephalus.*—A pathologic examination has been obtained in four cases of communicating hydrocephalus. Three of these have been studied in the above series and the fourth is a specimen which has been in the pathologic museum for several years. Because of the similarity of the findings in all cases, the results will be grouped and individual mention made only of accessory details.

Each of the four cases presented exactly the same pathologic condition — a barrier of very dense adhesions at the base of the brain. In each case the foramen of Magendie and one foramen of Luschka were sealed by adhesions and the other foramen of Luschka was patent to a certain degree, and through this single channel the fluid escaped from the fourth ventricle and therefore from the ventricular system. The adhesions completely encircled the brain anterior to the patent foramen of Luschka; and the basal cisternae — cisterna magna, cisterna pontomedularis, and cisterna interpeduncularis—were completely obliterated by these adhesions. The adhesions in each instance were most dense in the region of the medulla and cerebellum and became less pronounced in the chiasmal region. Minor adhesions were scattered over the surface of the brain. In one case the adhesions were present over the base, with additional dense adhesions completely binding the tentorium to the posterior surface of each occipital lobe, the superior surface of both cerebellar lobes, and completely encircled the midbrain as it passed through the opening in the tentorium cerebelli. In each instance an apparently complete encircling mass of adhesions sealed off the base of the brain so that the cerebrospinal fluid could not pass forward to the cerebral subarachnoid space, but only downward into the spinal canal. The obliteration of the various basilar cisternae, which are the centers from which cerebrospinal fluid is distributed over the cerebral subarachnoid space, may in itself be sufficient to eliminate the cerebral subarachnoid space from absorption, even without the encircling adhesions.

No doubt in many cases both foramina of Luschka may be obliterated, with a patent foramen of Magendie, or vice versa. In any case, the communication between the ventricles and subarachnoid space, though limited to one foramen at the base, is ample, being at least larger than the aqueduct of Sylvius. After passing from the ventricles, however, the absorption is limited to the *spinal* subarachnoid space and a minimal area of the subarachnoid space around the cerebellum.

The phenolsulphonephthalein tests show a reduction in absorption from the subarachnoid space to about one-fourth or one-fifth of the normal. This roughly corresponds to the diminution of the subarachnoid absorbing area due to the elimination of the cerebral subarachnoid space by adhesions.

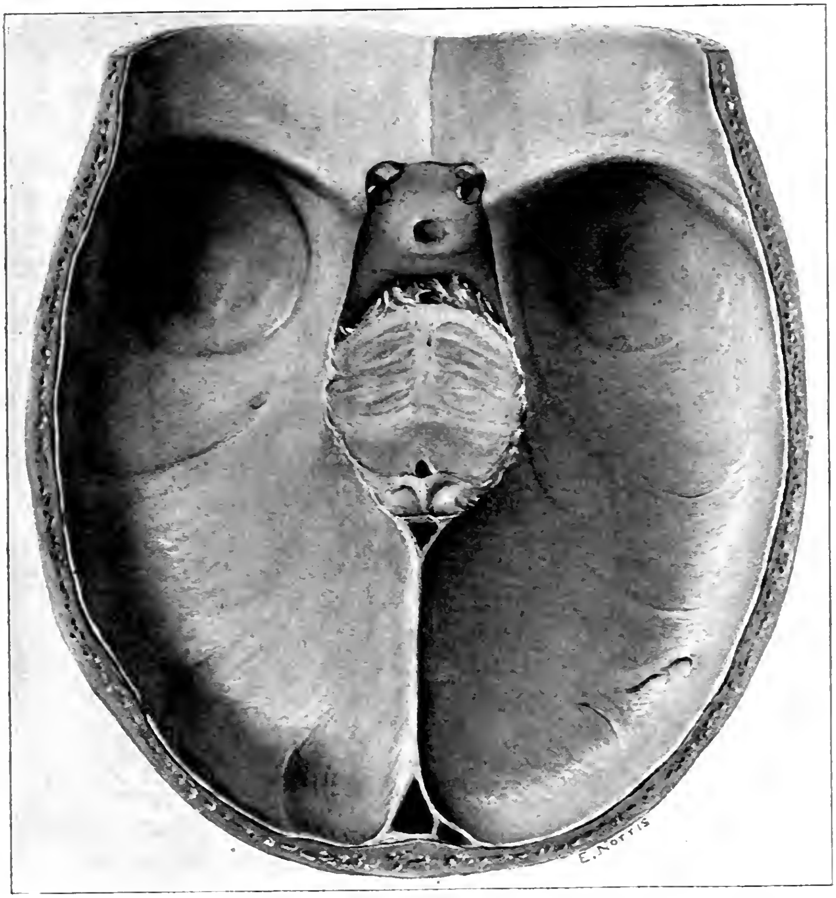

Fig. 4.—View of dura, showing midbrain passing from the posterior to the anterior fossa through the opening in the tentorium.

Note the adhesions between the periphery of the midbrain and the tentorium, also the dura along the base of the skull. The communication between the posterior and middle intracranial fossae is destroyed by these adhesions, and when this is true a communicating internal hydrocephalus results.

In each instance the adhesions between the brain and the dura were dense, necessitating their incision to prevent tearing the cortex during the removal of the brain. Special emphasis should be placed on the necessity of demonstrating the adhesions during the progress of the postmortem examination, for after they have been separated their

demonstration becomes difficult. This is especially true when the adhesions are thin and toward the periphery of their distribution. One not infrequently sees a large area of adhesions over the cerebral cortex which causes no internal hydrocephalus. This is probably due to the fact that the base is the distributing center for all the fluid that covers the brain, and the closure of the cisternae prevents the distribution, whereas a large cortical area can easily be compensated for by the normal excess of the absorbing area.

The presence of adhesions is responsible for the fact that fluid accumulates in the brain and not outside the brain, or, in other words, that an internal and not an external hydrocephalus results. This is because the brain is tightly bound to the dura, and more important, because the fluid-containing and fluid-absorbing subarachnoid space is obliterated over most of the brain, and especially at the distributing center in the cisternae.

The truth of the following paragraph from our former paper has been susbtantiated by the results of the pathologic examinations:

> We have had no pathologic examination on patients with hydrocephalus of the communicating type. It is very likely that the diminished absorption from the subarachnoid space is due to adhesions which diminish the size of the subarachnoid space. Adhesions anterior to the foramina of Luschka, by causing obliteration of the cisterna magna, would prevent the passage of fluid into the general cerebral subarachnoid space as effectually as if the aqueduct of Sylvius were obliterated. The two groups would then be essentially similar, differing only in the fact that the spinal subarachnoid space participated in absorption in the communicating type. . . . How much alteration in the meninges alone, without adhesions, interferes with absorption, cannot be stated. It seems to us probable that the major part if not all of the disturbance is due to the limitation of the subarachnoid space.

II. OBSTRUCTIVE INTERNAL HYDROCEPHALUS

A series of fifteen cases of obstructive internal hydrocephalus has been studied, in each of which the obstruction has been clinically demonstrated by the phenolsulphonephthalein test. In addition to these, numerous other cases have been observed in which tumors have caused the hydrocephalus, but they have not been included. Several other cases have been seen at necropsy, but are also not included because they were not previously observed clinically. In ten of these fifteen cases the obstruction has been verified by a postmortem examination. One was due to an acute tuberculous meningitis which sealed the foramina of Luschka and Magendie. Another case was an acute cerebrospinal meningitis in which the base was covered by exudate. Four cases had complete occlusion of the aqueduct of Sylvius, three of which showed histologic epithelial remnants of this structure, and the fourth was due to a solitary tubercle in the midbrain which had grown into and totally occluded the aqueduct of Sylvius. One of these

cases with iter obstruction had a second obstruction by adhesions, completely closing both foramina of Luschka and the foramen of Magendie. This child (N. M. 4) lived five years and was under observation most of that time, and despite an enormous hydrocephalus, did not lose all evidences of intelligence. At necropsy there was in

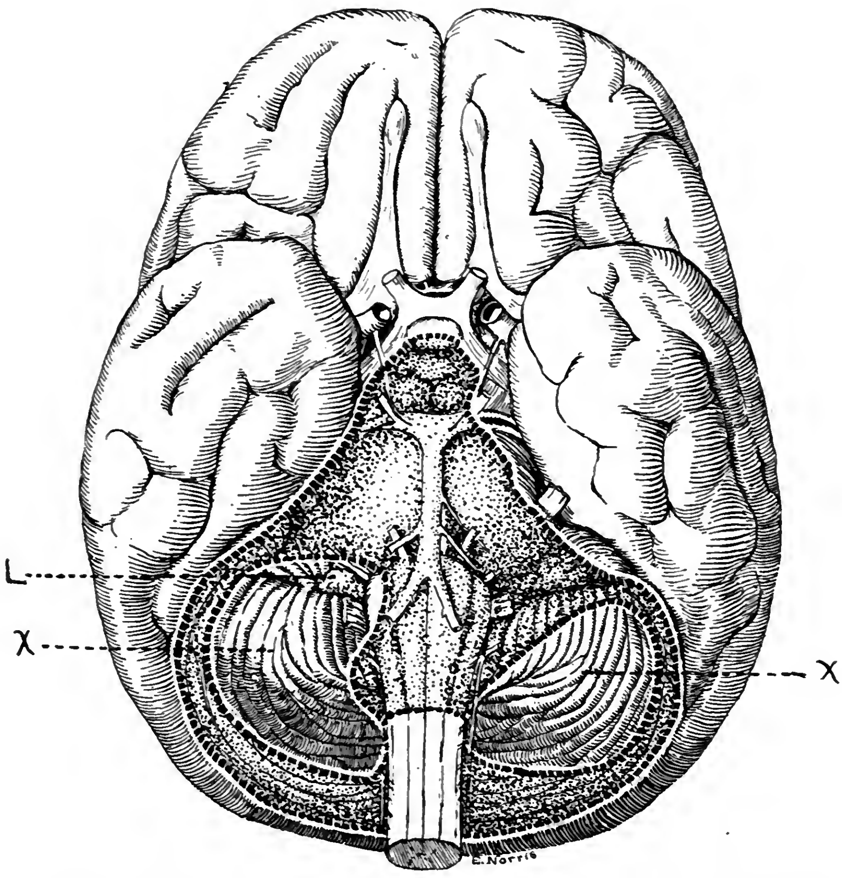

Fig. 5.—Diagram of the base of the brain, showing in diagram form, roughly, the distribution of the adhesions over the base of the brain responsible for the communicating type of internal hydrocephalus.

X, X represent areas on the cerebellar hemispheres which are relatively free from adhesions.

L represents the foramen of Luschka, which is patent only on this side. The opposite side is completely obliterated by adhesions. The adhesions extend along the tentorium on both the superior and inferior surfaces.

addition to the hydrocephalus a congenital urethral obstruction and a double hydronephrosis. The brain presented a great dilatation of the third and lateral ventricles anterior to an iter obstruction, and a dilatation of the fourth ventricle, anterior to the closure of the basal

foramina of exit. Adhesions between the cerebellum and dura no doubt restricted the dilatation of the fourth ventricle and mechanically prevented its enlargement into a great cyst. It was impossible to have suspected the presence of the second or iter obstruction. The obstruction at the base was certain because of the very scant amount of cerebrospinal fluid (2 to 4 c.c.) obtainable at successive lumbar punctures.

(*a*). *Demonstration of the Obstruction.*—In each of these fifteen cases, phenolsulphonephthalein failed to appear in the spinal fluid following its introduction into the lateral ventricle. In one instance (F. W. 6) a trace was present, appearing at some time in the interval between one-half and four and a half hours. Several months later the obstruction had become complete and phenolsulphonephthalein did not appear in the spinal canal. There was a corresponding reduction in the absorption from 2 to 1 per cent., and a corresponding increase in the appearance time. The significance of these observations will be mentioned later, in considering the interrelationship of the two types of hydrocephalus. In each of the fifteen cases the output of cerebrospinal fluid was under 2 per cent. as compared to the normal of 15 to 20 per cent., and readily explains the cause of the hydrocephalus. The spinal absorption in several cases was entirely normal; in several it was quite low, 10 to 30 per cent., as compared to the normal of 35 to 60 per cent. In these cases the amount of absorption is really immaterial in the production of the hydrocephalus, because the fluid never reaches the meninges. Its importance, however, is in the prognosis following operative intervention, for with a low spinal absorption (10 to 30 per cent.) the release of the obstruction would then transfer an obstructive hydrocephalus to a communicating hydrocephalus, and only modify but not cure the disease. It would only make its development less rapid.

The total time for elimination of the dye after ventricular introduction was studied in only a few cases, in each of which the excretion was carried over a period of several days; in one case eleven days on two different occasions. The excretion following spinal introduction varied from normal to two days, an index of which time is given by the two-hour output in the urine.

COMPARISON OF THE TWO TYPES OF HYDROCEPHALUS

Both types of hydrocephalus are due to a diminution in the absorption of cerebrospinal fluid. Both are obstructive, differing only in the location of the obstruction. In the so-called obstructive variety, the obstruction is within the ventricular system. In the so-called communicating hydrocephalus, the obstruction is in the subarachnoid space. In communicating hydrocephalus the obstruction is probably always the result of adhesions, which, of course, means that an inflammatory process has existed before birth if the hydrocephalus is congenital, or

it may develop at any time after birth. Such an inflammation of the meninges may seal the three foramina of exit from the fourth ventricle and produce an obstructive hydrocephalus, or it may leave one, two, or all the foramina patent and seal off the cisterna, producing the communicating type of hydrocephalus; or it is possible to do both; that is, the foramina may all be closed and the meninges sealed anterior

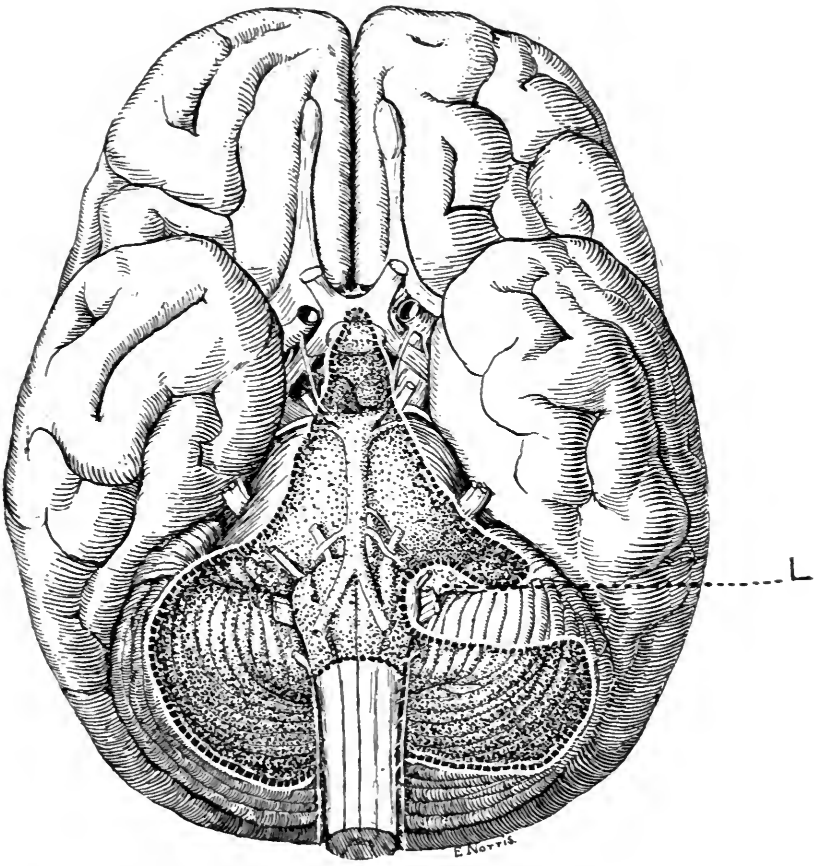

Fig. 6.—A diagram of the base of the brain showing roughly the extent of the adhesions at the base.

L is the patent foramen of Luschka, on one side only. The other foramen of Luschka and the foramen of Magendie are completely obliterated by adhesions. In this case the adhesions did not involve the tentorium, but only the base of the brain.

to the foramina. This, of course, would produce the obstructive hydrocephalus, and the meningeal obliteration, though of no consequence (because the fluid does not reach the meninges) could be demonstrated clinically only by tests as a greatly reduced absorption from the subarachnoid space. Case F. W. 6 is such an instance of a

combination of the two types. At first there was a minute and greatly delayed communication. The process was undoubtedly progressive, as later the obstruction became total and the absorption following ventricular introduction correspondingly diminished. In all of our cases of communicating hydrocephalus the foramen of Magendie has been closed, together with one foramen of Luschka. A gradual reduction in the size of the remaining foramen of Luschka would change the communicating hydrocephalus to obstructive hydrocephalus, as in the foregoing case, whereas clinically the transition would scarcely be noticed. It is, of course, of the greatest importance to determine whether the absorption from the subarachnoid space is normal or approximately so before attempting any operative procedure designed to relieve the obstruction. As mentioned previously, the transference from an obstructive to a communicating hydrocephalus would add but little to the patient's welfare.

MENINGOCELE AND INTERNAL HYDROCEPHALUS

The frequent association of a meningocele with internal hydrocephalus has long been known, and quite frequently an internal hydrocephalus has been observed to develop following the removal of a meningocele. This seems to us most probably due to the removal of the absorbing area of the meningocele, which was just sufficient (or nearly so) to maintain the balance between the production and absorption of cerebrospinal fluid. With its removal the production of fluid becomes sufficiently greater than absorption to cause increased dilatation of the ventricles.

In eleven patients with communicating hydrocephalus, three had a meningocele; and in fifteen cases of obstructive hydrocephalus, a meningocele was present in three. The formation of a meningocele in conjunction with a communicating hydrocephalus, arising in early intra-uterine life, seems explainable by the pressure which causes the cerebrospinal fluid to take the path of least resistance, usually in the lumbar region, which is the last part of the spinal canal to be bridged over. The presumption is natural that a meningocele signifies an increased pressure of cerebrospinal fluid in the spinal canal, or a communicating hydrocephalus. But that this is not necessarily true is shown by its existence in three cases of obstructive hydrocephalus. In one, however, the hydrocephalus was originally of the communicating variety, and when first seen by us was in the last stages of the transition to a total obstruction. The other case was a myelocystocele, the cerebrospinal fluid having no communication with the sac, which was now blind, and even the original communication with the central canal of the spinal cord was closed in several places. The relationship of the meningocele to the obstructive hydrocephalus in the remaining

case could not be ascertained because of the absence of a pathologic examination.

In all cases with a meningocele which have recently come under our observation, careful studies have been made of the amount of absorption from the spinal canal in addition to other evidence of internal hydrocephalus. Only in those cases in which a normal absorption is present from the spinal canal have we removed the meningocele, and in these cases have observed no subsequent secondary effects on the brain. The phenolsulphonephthalein output from the spinal canal we regard as a thoroughly reliable index of the function of the meninges, and know of no other way in which a safe decision can be made in the operative treatment of a meningocele.

THE RELATION OF MENINGITIS AND OTHER FACTORS TO INTERNAL HYDROCEPHALUS

It is our opinion, based on the clinical studies and pathologic findings, that the great majority of cases of hydrocephalus result from meningitis. A hydrocephalus of short duration may occur during the meningitis, due to the tubercle bacillus, the pneumococcus, and doubtless other organisms. Chronic hydrocephalus is to be expected only following a meningococcus meningitis. That a very mild form of what was probably meningococcus meningitis has been the cause of a number of our cases seems evident from some of the history, but the illness has been so slight and recovery so prompt that the mother has looked on it as a "cold," "stomach trouble," or some illness incident to teething, and it is only by careful questioning that the illness is recalled. Yet after these mild symptoms hydrocephalus may result.

At necropsy adhesions are found which have the usual basal distribution of other types of meningitis, and these adhesions are the cause of the internal hydrocephalus. At necropsy exactly the same findings are obtained in cases which have an internal hydrocephalus at birth; that is, adhesions over the same general distribution, affording proof of the existence of an intra-uterine inflammatory process. What organism is responsible for these lesions is entirely unknown. So is also the organism that causes intra-uterine lesions of other serous membranes. In no instance have we been able to elicit any illness of the mother occurring during gestation which could account for the meningitis in the child.

An analysis of the accompanying table (Table 3) shows the high percentage of cases in which meningitis is the basis for the hydrocephalus. The figures are intended only to give the results from a small group of cases and may no doubt be greatly altered with increasing numbers. Both types of hydrocephalus are caused by this process, as heretofore mentioned. It is really difficult to understand how the

TABLE 3.—Summary of Etiologic Factors in Cases of Internal Hydrocephalus

Hydrocephalus	Meningitis			Congenital Malformation; Not Inflammatory	Tumor	Uncertain Whether Congenital or Inflammatory Process; Foramina at Base Occluded	No Proof of Character of Lesion Because no Examination
	Clinical Alone	Necropsy or Operation Alone	By History and Operation or Necropsy				
Obstructive	2	2	3	3	1	1	3
		46.6%		(20%)	(6.6%)	(6.6%)	(20%)
Communicating	4	3	..	..	..	..	4
		63.6%					(37.4%)

Excluding those cases in which no evidence is obtainable because of absence of examination by operation or necropsy:

1. The percentage of meningitis cases in obstructive hydrocephalus is 58.3 per cent.
2. The percentage of meningitis cases in communicating hydrocephalus is 100 per cent.
3. The percentage of meningitis cases in both obstructive and communicating hydrocephalus is 80 per cent.
4. The percentage of congenital malformation causing hydrocephalus (in all cases) is 15.8 per cent.; and excluding communicating hydrocephalus, is 25 per cent.

communicating hydrocephalus can be caused by any other process than a meningitis, because of the rather diffuse area necessary to be invaded to produce these results. In the series of eleven cases of communicating hydrocephalus, four gave a definite history of meningitis, but from these no anatomic examinations were possible; three others gave no history of meningitis, but the condition was evidently congenital, because each had a lumbar meningocele and at necropsy each of these gave all the evidences of an old extensive basilar meningitis. Of the four remaining cases in this group, three were evidently of congenital origin, the enlargement of the head being noticed very shortly after birth, and the fourth was noticed when the child was 3 months old and may also have been congenital, no illness having been noticed between the time of birth and the enlargement of the head. As an anatomic examination was not made in any of these four cases, the etiology remains entirely obscure.

Two cases of obstructive hydrocephalus (M. R. 4 and R. C. 8) present an almost indistinguishable anatomic picture. In each patient the foramen of Magendie and both foramina of Luschka were entirely absent, and the posterior fossa was filled with a cyst, resulting from a dilated fourth ventricle. The other ventricles were proportionately dilated. In one of these cases the child was perfectly normal until four

months old, when a typical mild meningitis developed. The hydrocephalus followed immediately. At necropsy only a few minor adhesions were found. Had not the history been definite, the condition could easily have been regarded as congenital and the foramina at the base as congenitally absent, but the condition was unquestionably due to the meningitis, few traces of which remained. The other case with a similar anatomic picture was of congenital origin and the foramina were likewise closed. Whether an intra-uterine inflammatory process caused the condition similar to the extra-uterine meningitis of the other case, or whether the foramina were congenitally absent, could not be decided.

Congenital obliteration of the aqueduct has been adequately presented in the previous paper. Recently, Schlapp and Gere[1] presented additional cases of the same character.

One tumor has been included in this series. Tumors, of course, with rare exceptions, produce only the obstructive type of hydrocephalus. In infancy they are extremely rare and it is only in early childhood that this becomes an important factor to consider. As age increases hydrocephalus becomes more the result of tumor and relatively less the result of meningitis, on account of the increasing frequency of tumors.

SPONTANEOUS CURE OF INTERNAL HYDROCEPHALUS

Spontaneous recovery is not infrequent in internal hydrocephalus. This is evident from the cases seen from time to time of arrested growth of the abnormally large head. We have at least three cases under observation in which the diagnosis is clear, and in which there has been no change in the size of the head of the patient for years. Another child was studied through an attack of meningitis into the stage of hydrocephalus. After being lost sight of for three years, she returned apparently entirely cured. Many patients with meningitis recover without an internal hydrocephalus, and no doubt many cases of hydrocephalus follow meningitis and sooner or later recover.

Spontaneous recovery naturally depends on the cause of the disease. A spontaneous cure in a case of hydrocephalus with a congenital or other obstruction at the aqueduct seems entirely impossible, but it is not difficult to imagine recovery following the gradual disappearance of adhesions. This is especially true when one realizes how adhesions may disappear. The reverse may also be true and adhesions in the meninges as elsewhere may be progressive and increase the hydrocephalus. It is also possible to imagine a sudden rupture of the thin

1. Schlapp, M. G., and Gere, B.: Occlusion of the Aqueduct of Sylvius in Relation to Internal Hydrocephalus. Am. Jour. Dis. Child., 1917, **13**, 461.

wall of a large fourth ventricle cyst, producing a new foramen of exit to the subarachnoid space. It is not improbable that the majority of cases having a meningocele but no hydrocephalus, represent a regressive stage or cure of an old intra-uterine hydrocephalus. Otherwise it is difficult to understand the formation of many meningoceles.

SUMMARY AND CONCLUSIONS

1. Twenty-six cases of internal hydrocephalus have been studied, fifteen of the obstructive and eleven of the communicating variety.

2. These cases have been studied with intraventricular and intraspinal injections of phenolsulphonephthalein.

3. Postmortem examinations have demonstrated an obstruction in every case in which an obstruction has been shown clinically by this test. The obstruction may be a congenital malformation or inflammatory process or tumor, and occur at any part of the ventricular system, but usually at the aqueduct of Sylvius or the foramina of Luschka and Magendie.

4. In all cases of obstructive hydrocephalus there is practically no absorption from the ventricles, and frequently (although not necessarily) a normal absorption from the subarachnoid space. Hydrocephalus results because the fluid is mechanically prevented from passing from the ventricles, where the fluid forms, to the subarachnoid space, where it is normally absorbed, and where only it can be absorbed.

5. Communicating hydrocephalus is caused by a barrier of adhesions at the base of the brain which mechanically prevents the cerebrospinal fluid from reaching the cerebral subarachnoid space, where the greatest part of absorption normally takes place. The various cisternae or centers for the distribution of cerebrospinal fluid are more or less obliterated by adhesions.

6. Absorption of cerebrospinal fluid is a general process, from the entire subarachnoid space, and communicating hydrocephalus results because only a fraction of this area can be utilized for absorption.

7. These pathologic findings harmonize with the clinical phenolsulphonephthalein tests, which show a greatly diminished absorption from the subarachnoid space.

8. Obstructive and communicating hydrocephalus are, therefore, essentially the same, and in reality all are due to obstruction. In the obstructive variety the obstruction is in the ventricular system; in the communicating variety the obstruction is in the subarachnoid space.

9. Obstructive hydrocephalus may, by operation or spontaneously, change to communicating hydrocephalus, or the reverse may occur spontaneously. Careful studies with the phenolsulphonephthalein test will indicate these possibilities.

10. Meningitis is by far the greatest etiologic factor in both types of hydrocephalus and probably always causes the communicating variety. This may be either prenatal or postnatal. The meningitis may be of a very mild grade and easily overlooked.

11. There is a definite relationship between a meningocele and internal hydrocephalus; both usually probably result from the same cause. The removal of a meningocele may aggravate a fairly well balanced or even arrested case of internal hydrocephalus. This probably results from a diminution of the absorbing area.

12. Spontaneous recovery of internal hydrocephalus sometimes occurs.

13. We feel that the surgical treatment of internal hydrocephalus has now a definite anatomic basis and hopeful prospects. The operative results of a series of cases will appear in a subsequent communication.

A MENTAL AND PHYSICAL SURVEY OF A GROUP OF JUVENILE DELINQUENTS

WITH NOTES ON THE YERKES-BRIDGES POINT SCALE *

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At the request of the Boys' and Girls' Aid Society of San Francisco we undertook in September, 1916, a study of the boys placed in the society's care by the various juvenile courts of California. A few of these were committed as orphans or destitute, but the great majority were committed to detention because of truancy, incorrigibility or active crime.

Our study had for its primary purpose the disclosure of physical and mental defects, but was later extended, with the assistance of Miss Annette Rosenshine, to an investigation of the home conditions of the mentally normal or dull normal boys.

We have also taken this opportunity to compare the Yerkes-Bridges Point Scale with the Binet-Simon Scale (1911 Goddard revision) and to compare the physical measurements with the mental tests, following in some respects the recent work of Doll.

Our physical examinations were made according to the routine of the Stanford Children's Clinic, and included investigations of the skin, eyes, ears, teeth, tonsils, pharynx, thyroid gland, lungs, heart, abdomen, genitals and extremities; the tendon reflexes, and the posture. In addition, vision was tested by the Snellen card at 20 feet without glasses, and a rough estimate of hearing was obtained by the watch test. The Wassermann test was applied in sixty cases, including about half of those in which enlarged epitrochlear glands were found, but owing to circumstances not under our control, could not be carried out in the remainder. Measurements of standing height, chest circumference, head circumference, and of the grip of each hand (dynamometer) were made. It is a matter of regret that the inconvenience of transporting our spirometer to and from the home of the society made it impossible to obtain measurements of vital capacity.

GENERAL PHYSICAL ABNORMALITIES OF THE GROUP AS A WHOLE

Taken as a whole, the 110 boys first examined were somewhat below the normal in height, with a percentile[1] of 44, as compared with the normal average of 50. The percentile for weight, however, was

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* From the Department of Pediatrics, Stanford University Medical School.

1. All percentiles were calculated from the Smedley tables, in which the group average is 50, with a minimum normal of 0 and a maximum normal of 100.

57 and the percentiles for right and left grip were 55 and 59, respectively, all of which are well above the normal. The superiority of the left grip is noticeable. Of the boys, 18.4 per cent. showed vision below 20/30 for the right and 25.2 per cent. for the left eye. Strabismus — convergent except in one instance — was found in 10 per cent. Defective hearing occurred in 15.4 per cent. The teeth were decayed in 53 per cent., irregular or maloccluded in 7.3 per cent. and merely dirty in 11.2 per cent. The tonsils were enlarged in 36.4 per cent. and had been removed in 11.7 per cent. Enlargement of the thyroid gland was not encountered. The anterior cervical glands were palpable in 61 per cent., the posterior cervical in 50 per cent., the inguinal in 74.5 per cent., the axillary in 50 per cent. and the epitrochlear in 19.1 per cent. Wassermann tests were made in ten of the twenty-one cases in which the epitrochlears were palpable without a single positive reaction being obtained. In the one case, out of the sixty tested, in which a positive reaction did occur, the epitrochlears were not palpable. Our respect for this time-honored sign of syphilis has been lessened. Abnormalities of the chest, noted as "flat," "narrow," "pigeon-breasted," occurred in 10 per cent. Two cases of chronic endocarditis were found. One inguinal hernia was discovered. The prepuce was elongated or adherent in 21.7 per cent., and had been circumcized in 20.9 per cent. Four instances of unilateral cryptorchidism were found. Pubic hair was present in 54.5 per cent. Disease of the skin — acne, furunculosis or impetigo — occurred in 10.9 per cent. The knee jerks were unusually lively, without other signs of spasticity, in 6.4 per cent. Postural defects — round shoulders, wing scapulae, lateral curvature of the spine — were noted in 22.7 per cent.

Taken as a whole, and leaving aside for future consideration the various measurements and certain special features, the physical defects are those common to any group of children whose hygiene has been long neglected.

MENTAL EXAMINATION

At the time when the present study was begun, the children's clinic was considering the merits of the Yerkes-Bridges[2] Point Scale, and for purposes of comparison a majority of the boys, ninety-eight in all, were examined both by the Binet-Simon Scale (1911 Goodard revision) which had been used hitherto in the clinic, and by the Yerkes-Bridges Scale.

The Yerkes-Bridges Point Scale was devised by Robert M. Yerkes, assisted by James W. Bridges, following a suggestion by the late Dr. E. B. Huey. A complete description of it was published in 1915 by Yerkes, Bridges and Hardwick.[2] The purpose of the authors was to construct a new scale to

2. Yerkes, R. M., Bridges, J. W., and Hardwick, R.: A Point Scale for Measuring Mental Ability. Baltimore, Warwick and York, 1915.

supplant the Binet-Simon Scale and its various revisions, which had been found by many workers to be unsatisfactory. They included, however, a considerable number of the Binet tests in their own method. The difference between the two scales will be best indicated by a brief description of each.

The Binet Scale, as well as its revisions, presents a series of tests arranged in order of presumably increasing difficulty, and divided in groups of four or five, each group corresponding with a year of "mental age." The mental age of the subject of the examination is that corresponding to the highest complete group of tests that he passes, plus the figure for the number of tests, expressed as fifths of a year, that he passes in the higher groups. Thus, if a child passes all the tests up to and including Group X, three tests in Group XI, and one test in Group XII, his mental age is stated as $10\frac{4}{5}$ $(10+\frac{3}{5}+\frac{1}{5})$. In this scheme it is theoretically assumed that (1) each group of tests examines satisfactorily for the age the various mental functions; (2) that every "normal" child without regard to environment or training can answer all the questions assigned to his physical age; (3) that inability to answer perfectly any question or test implies complete failure in that test; (4) that all tests are of mathematically equal weight in evaluating intellectual capacity. As a matter of fact—and this is an important objection to the Binet system—every examiner is compelled to modify to some extent the result of every examination by taking into account certain extraneous factors, such as language difficulty, unfavorable environment, and so on. The personal equation, therefore, enters into all Binet testing, and to an undesirable extent.

The Point Scale presents a series of tests, arranged roughly (for the sake of convenience only) in order of difficulty but not divided into age groups, which are designed to test the various mental functions, such as auditory memory, motor coordination, ideation, kinesthetic discrimination, logical judgment. To each of these tests a certain value, expressed in points, is attached. The sum of these values, that is, the score attainable by completion of all tests, is 100. The score attained by the individual examined is the sum of the points assigned to the tests in which he is successful. Part credit is given for partial completion of the tests, thus abandoning the all-or-none principle of the Binet system. The final score is then compared with the norm. This norm is properly made a variable quantity, allowance being given for favoring or unfavorable circumstances of environment and training, factors which practically all investigators recognize as influencing the capacity of individuals to pass mental examinations. The "setting" of the norm, however, can be determined by a direct comparison of the scores of other individuals belonging to the same group and need not be left to the personal judgment of the examiner. The Point Scale offers both an absolute scale of measurement—in relation to an ideal 100—and a relative scale—in relation to the norm for the particular social or educational group to which the individual belongs. The improvement over the older scale is thus in the direction both of objectivity and of flexibility. As the authors point out, the results of examinations at the hands of different examiners are directly comparable, and at the same time the norms can be constantly corrected by experience and comparison.

The discrepancies between the two methods of examination, shown graphically in Chart 1, are considerable and of rather serious significance. In adopting norms for the Point Scale it must be emphasized that we do this only for comparison with the Binet Scale, and that, to our mind, norm-comparison is not the chief purpose of the Point Scale, which has its greatest value rather in estimating total mental capacity. The point scale, as has been pointed out by its originators, has the advantage of being self-perfecting and is not committed to

rigid norms, so that we have taken the liberty of modifying the original figures of Yerkes and Bridges by comparison with those of Haines,[3] derived from a study of individuals belonging to about the same social stratum as the one with which we were dealing, and with data of our own. The norms for ages above 15 cannot be regarded as fully established: those we have adopted are based partly on the Yerkes-Bridges figures and partly on data of our own, and must be taken as only approximations, with an error of perhaps 3 per cent.

We suggest that the originators of the point scale are rather too conservative in stating that the scale is not of great value above age 16. We have a conception, which may or may not be correct, that the scale tests with considerable completeness and accuracy what we may call basic intelligence. By this we mean the broad foundation of

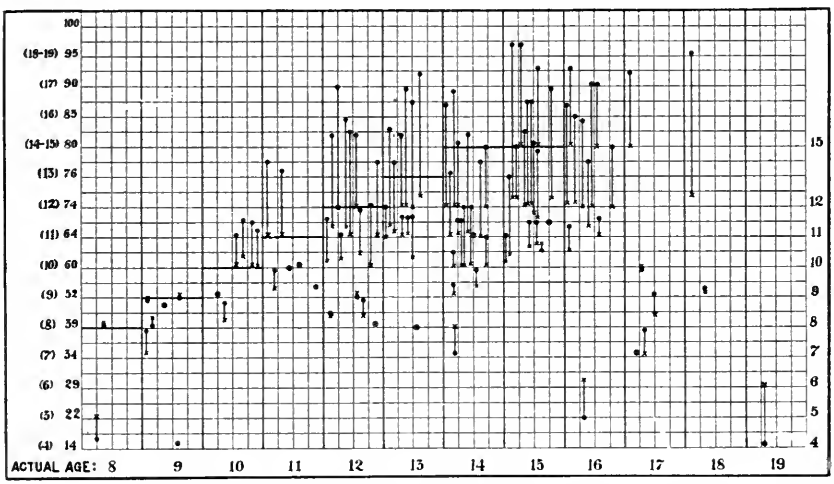

Chart 1.—Comparison of the Yerkes-Bridges Point Scale score and the Binet age of ninety-eight delinquent boys. The Point Scale score and Binet age of each boy are connected by a vertical line. Point Scale score = ●; Binet age = ×.

mental endowment which every normal person must possess before he can branch out into the more highly specialized, so-called higher intellectual functions of adult life. Above this basic level, which is common to all normal individuals, mental growth is along the line of special acquirement and follows closely educational direction. Therefore we feel that so-called adult tests are rather impracticable except along special lines, but that basic intelligence can be tested at any age and is of value at any age.

Our Binet tests — Goddard's 1911 revision with tests for age 15 and for the adult — were practically useless above age 12, and were

3. Haines, T. H.: Mental Examination of Delinquent Boys and Girls. Illinois Med. Jour., 1915, **28**, 283.

also very defective for age 11. This is in accordance with the experience of most investigators. It is plain from Chart 1 that a Binet age of 12, or 12 and a fraction, may represent widely varying degrees of intelligence, as measured by the Point Scale. That the Goddard tests for age 15 and for the adult fail to remedy the fault is also clear.

In Chart 2 we have compared all our scores (calculated as intelligence quotients[4]) by the two scales, arranging them in an ascending order of the Point Scale intelligence quotient. Up to 0.90 the discrepancies nearly balance, the Binet quotient being higher in 17, and the Point Scale higher in 19. At 0.65 and below (P. S. I. Q.) (that is, in the unquestionably defective group) nine Point Scale quotients are lower, and only two Binet quotients are lower, two being the same. Above 0.90 (P. S.) *only one* Binet quotient was higher (by 0.03).

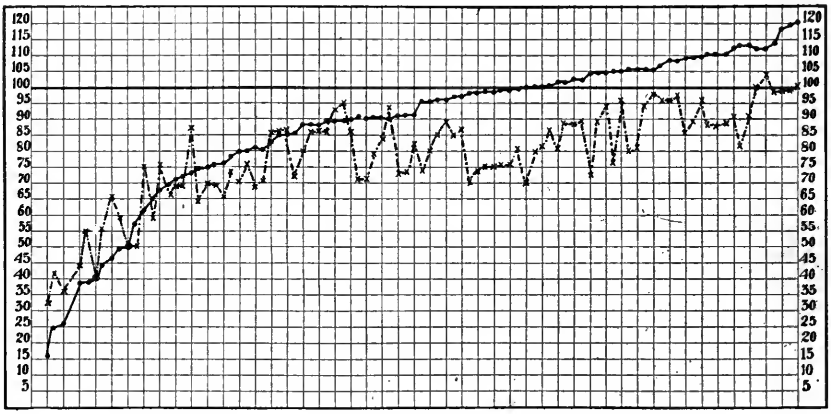

Chart 2.—Comparison of all Point Scale and Binet intelligence quotients arranged in ascending order of Point Scale quotients. In this and following charts ● = Point Scale intelligence quotients; X = Binet Scale intelligence quotient.

Considering a Point Scale quotient of 1.10 or more as evidence of mental superiority, we find in this group that the Binet quotient gave no indication whatever of such superiority; three out of five cases with the highest P. S. quotients were actually below 1.00 by the Binet, and only one was above 1.00.

Charts 3 and 4 are arranged to show the degree of "overlapping" between groups by the two scales. Kohs[5] has already drawn attention to this phenomenon. We have provisionally adopted a maximum of 0.95 for the dull normals, instead of 0.90 as generally used for the

4. The intelligence quotient equals the mental age divided by the actual, or chronological, age.

5. Kohs, S. C.: The Borderlines of Mental Deficiency. Jour. Psycho-Asthenics, 1916, **20,** 63.

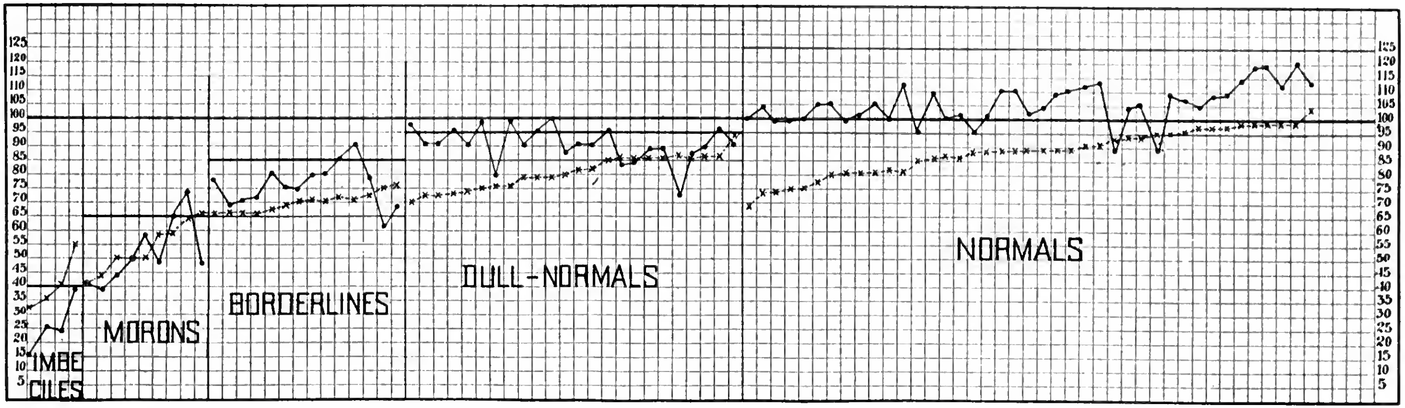

Chart 3.—Comparison of Binet Scale and Point Scale quotients arranged on the basis of Binet quotient.

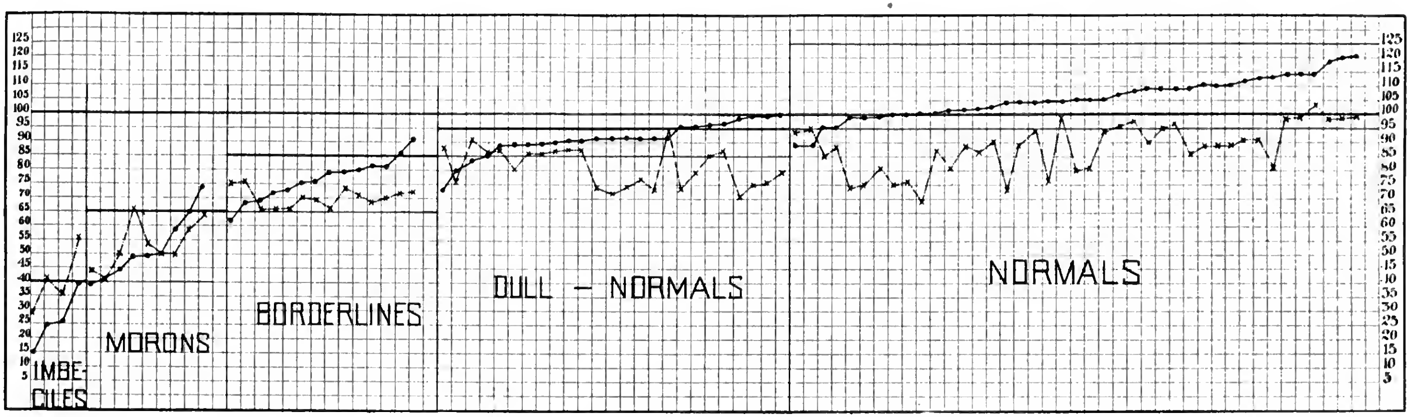

Chart 4.—Comparison of Binet Scale intelligence quotients arranged on the basis of Point Scale quotient.

Binet Scale. Table 1 shows the amount of "overlapping." The significant feature of this table is that by the Binet Scale, forty-two boys, who, we were satisfied, belonged to the normal group, had intelligence quotients below the group in which they were placed, whereas by the Point Scale eleven ranked above and only five below. Stated in another way, by the Binet tests, we should have had to place thirteen boys in the borderline group instead of in the dull normal group, whereas by the Point Scale only three such changes would have been necessary, if the results were to be rigidly interpreted by the intelligence quotient.

Let us emphasize again that the intelligence quotient, being based on group average norms in neglect of individual variations, involves a good deal of unavoidable error and to our mind should be used only for purposes of group study.

TABLE 1.—Showing Comparative Amounts of Overlapping by the Two Scales

Cases	Binet Scale		Point Scale	
	Above	Below	Above	Below
Imbeciles, 15-40	2	0	0	0
Morons, 40-65	1	0	1	1
Borderlines, 65-85	0	0	2	1
Dull Normals, 85-95	0	13	8	3
Normals, 95	..	29	..	2
Total	3	42	11	7

Now it must be clear that one or the other of the scales is seriously faulty. That the Binet scale is at fault is suggested by the character of the discrepancies. In the first place, in unquestionably defective children the Point Scale gives a lower rating. Second, the discrepancies are least at the ages 6 to 10, when the Binet Scale has already been recognized as most accurate. Third, in the higher ages, when the Binet Scale has been found to be unsatisfactory, Point scores are obtained that correspond with normal expectation and in normal children increase with age (exception, at ages 14 to 15, when the score is stationary). Fourth, indications of exceptional intelligence are obtained by the Point Scale and not by the Binet Scale, which have been corroborated in a few of our cases by strong collateral evidence.

The Point Scale, moreover, appeals strongly to those who dislike the indirection of the Binet plan of scoring. To us the latter seems perfectly analogous to the recording of height, for instance, in terms of age. Besides being scientifically objectionable because indirect, it is also essentially inaccurate because it fails to take into account

the considerable variations of intelligence existing among normal individuals. Certainly but a small percentage of the many examinations that we have made during the last four years by the Binet Scale have shown an exact correspondence between mental "age" and chronological age.[6] The Point Scale score, on the other hand, is a direct statement of measurement and approaches the ideal of recording data in absolute rather than in relative terms.

We cannot leave the subject without mentioning a point which experience has brought frequently to our attention. This is the caution which is necessary in comparing individual scores with group average norms, as in the intelligence quotient, for the benefit of parents, guardians or teachers. We feel that in so doing the normal variations are frequently lost to sight and the stigma of retardation or pathologic deficiency wrongly fastened on the subject. It must be remembered that while the examiner can make allowances for normal variation, the laity will not do so. The figures for mental age are too readily compared with chronological age and insignificant degrees of variation require explanation which often serves only to cast suspicion still further. That this is by no means an unimportant or merely academic point is indicated by the strong public prejudice already created in many quarters against public school mental examinations. This is a question which must be promptly faced if mental examinations are to be generally introduced in American schools. The noncommittal (and more accurate) Point score has the inherent advantage that it can always be compared with *minimum* normal figures for age, instead of with a group average norm.

A word as to our method of deciding on the final diagnosis: We have not depended entirely on the score attained by either scale, but in a few instances have had to make allowance for various retarding environmental influences, such as deafness, faulty vision, and especially the effects of isolation and imperfect adaptation to surroundings consequent to foreign birth, foreign parentage and imperfect use of English. For these reasons, a few individuals have been provisionally placed in a category above that for which a strict interpretation of the tests would qualify them. In a few instances, also, we have modified the Point Scale diagnosis by a *favorable* discrepancy in the Binet Scale, but this has been necessary in but few cases.

PHYSICAL FINDINGS COMPARED WITH MENTAL STATUS

In Tables 2 and 3 we have arranged the more significant physical findings in columns parallel with our mental examinations. For this purpose we have taken ninety-three cases selected because of completeness, but on no other basis of exclusion.

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6. Yerkes, Bridges and Hardwick (p. 40) (Footnote 2) by a reconstruction of Goddard's data have brought out the same point very forcibly.

TABLE 2.—Summary of Physical—

	No.	Offense	Actual Age		Height		Height Percentile	Weight		Weight Percentile	Grip		Grip Percentile		Head		
			Yrs.	Mos.	In.	Mm.		Lbs.	Kg.		Right Kg.	Left Kg.	Right	Left	Girth, Cm.	Excess, Cm.	Deficit, Cm.
	4	Stealing	17	1	66¼	1,680	43	138¾	63.0	66	41	42	30	47	55.5	....	....
	5	Stealing	12	3	61½	1,562	95	112	50.8	94	39	38	102	110	.....	....	....
	6	Incorrigible	15	4	66¼	1,680	79	138	62.5	85	46	46	87	91	56.9	2.2	....
	9	Dependent	15	11	64	1,625	57	133¼	60.4	88	39	41	65	83	58.5	3.5	....
	10	Dependent	10	9	55⅛	1,400	86	70½	31.8	74	19	22	70	93	53.5	0.7	....
	14	Stealing	16	2	60¾	1,545	10	105½	47.8	17	19	25	02	09	53.5	....	1.6
	15	Incorrigible	11	9	52⅝	1,337	27	69	31.3	41	20	22	60	85	51.5	....	1.6
	19	Stealing	15	5	67⅛	1,705	87	142½	64.5	91	38	32½	60	51	.....	....	....
	20	Incorrigible	16	3	64	1,630	34	131½	59.6	73	36	34	30	30	54	....	1.2
	26	Dependent	10	..	54⅞	1,395	84	79¼	35.8	91	16	21	30	92	52.2	....	0.7
	27	Stealing	13	7	55⅝	1,410	14	78½	35 5	22	23½	22½	43	48	53.6	....	....
	28	Truancy	15	6	63¾	1,622	55	122¼	55.5	74	42	35	77	60	.....	....	....
	29	Stealing	11	5	55¼	1,405	70	72½	32.8	58	22	15	75	20	51	....	2.0
	35	Stealing	16	3	62¾	1,595	20	111½	50.5	29	....	....	....	....	.....	....	....
	37	Truancy	12	4	53⅝	1,362	20	83¾	37.9	71	24	22	70	70	54.3	1.0	....
	38	Dependent	12	5	59½	1,512	90	97½	44.2	91	29	23	91	75	52.5	....	0.8
	39	Dependent	12	8	58¼	1,480	80	96¾	43.8	91	31	27	93	91	55	1.7	....
	40	Dependent	13	7	61⅞	1,575	85	89¼	40.4	58	26	24	60	60	53.7	....	....
	41	Stealing	10	6	51⅝	1,312	36	70	31.7	73	20½	19½	83	83	52.8	....	....
	42	Burglary	16	8	60	1,525	32	96	43.5	08	35	33	25	27	52.3	....	3.1
Normals	43	Truancy	12	5	55	1,400	39	92	41.7	86	25	28	75	95	54	0.7	....
	47	Dependent	13	..	54	1,378	08	74½	33.7	13	27	32	65	91	53.3	....	....
	57	Incorrigible	15	7	63⅞	1,625	57	119	53.9	68	30	31	30	45	54.5	....	0.8
	59	Stealing	14	..	57⅞	1,470	21	83	37.6	19	25	26	35	50	53.3	....	0.6
	62	Incorrigible	14	8	61	1,552	51	97½	44.2	50	30	29	60	65	53	....	1.8
	63	Burglary	15	7	62	1,575	35	134¼	61.0	88	41	40	73	81	54.3	....	0.4
	67	Incorrigible	14	2	61	1,552	51	112½	51.0	80	42	39	91	92	55	1.0	....
	69	Stealing	15	4	61⅛	1,555	27	107	48.5	41	39	44	65	88	51.3	....	3.4
	72	Truancy	8	7	47¾	1,215	39	52¼	23.7	37	16	15	77	77	49.5	....	2.7
	76	Truancy	10	7	51½	1,310	34	75¾	34.3	88	20	18	80	70	52.8	....	....
	79	Neglect	13	1	62¼	1,580	85	93¾	42.4	67	26	25	60	65	53.9	0.5	....
	82	Truancy	14	3	57¼	1,455	16	92	41.7	38	38	34	86	85	55	0.9	....
	83	Truancy	14	..	62¼	1,582	66	104	47.2	66	35	31	80	75	52	....	1.9
	87	Burglary	15	3	70¼	1,785	96	151¼	68.2	92	56	53	94	95	56	1.4	....
	91	Stealing	12	..	55⅞	1,420	50	73	33.1	32	24	23	70	75	51.5	....	1.7
	92	Stealing	16	4	67	1,705	70	125¼	56.8	57	34	38	20	50	53	....	2.2
	97	Incorrigible	9	8	53½	1,360	87	62½	28.3	62	21	21	91	93	50.6	....	2.0
	106	Stealing	13	9	58⅞	1,495	55	88¾	40.2	57	30	24	80	60	54	0.3	....
	107	Stealing	13	..	59¾	1,520	67	102	46.2	84	39	36	92	93	52	....	1.4
	108	Stealing	10	8	51¾	1,315	28	71¾	32.5	80	22	17	90	60	49.5	....	3.3
	110	Incorrigible	11	2	55⅝	1,415	75	83¾	38.0	90	24	23	85	90	51.5	....	1.4

—and Mental Findings

Vision O. D.	Vision O. S.	Strabismus	Defective Hearing	Enlarged Tonsils	Teeth	Lymph Nodes Cervical	Lymph Nodes Epitrochlear	Prepuce	Testes	Skin Disease	Postural Defects	Point Scale Score	Binet Age	Normal = 100 Binet I. Q.	Normal = 100 Point Sc. I. Q.	Physical Percentile (Normal = 50)
20/20	20/20	0	0	+	0	+	0	0	0	Fur.	0	96	15	88	100	26
20/20	20/20	0	0	0	0	0	0	0	0	0	0	88	12	98	119	98
20/20	20/20	0	0	0	0	0	0	R.	0	Acne	0	97	15.2	99	118	86
.....	.....	0	0	+	0	+	0	0	0	0	0	89	12.6	79	105	73
20/20	20/20	0	0	+	0	0	0	R.	0	Im.	0	67	10	93	106	81
20/20	20/20	0	0	0	0	+	0	0	0	0	0	93	15.4	95	108	10
20/20	20/20	0	0	0	D.	+++	0	Lg.	0	0	0	76	11.4	97	106	53
.....	.....	0	0	+	0	+	0	0	0	Im.	0	87	12.4	81	106	72
20/20	20/20	0	0	0	D.	0	0	0	0	0	0	85	12.4	71	99	42
20/20	20/20	0	0	0	D.	+	L. +	0	0	0	W.S.	68	10.4	96	118	74
20/20	20/20	0	0	+	D.E.	++	0	Lg.	0	0	W.S.	89	12.2	90	112	32
20/20	20/20	0	0	+	0	+	+	0	0	0	0	87	12.4	72	106	67
20/20	20/20	0	+	0	D.	++	0	Lg.	0	0	L.C.	79	11.2	98	114	56
20/20	20/20	0	0	0	D.	0	0	0	0	0	0	84	12	74	98	25
.....	.....	0	0	0	D.	+	0	Lg.	0	0	0	83	11	90	111	58
20/40	20/100	0	0	0	D.	0	0	0	0	Im.	0	72	10.6	86	96	87
.....	.....	0	0	0	0	0	0	0	0	0	0	78	11.4	89	104	89
20/20	20/20	0	0	0	D.E.	0	++	0	0	0	0	87	12	88	111	66
20/20	20/20	0	0	0	D.	++	0	R.	0	0	0	65	10.4	100	105	69
20/20	20/30	+C.	0	0	D.	0	0	0	0	Warts	W.S.	91	15	90	103	23
20/20	20/30	+C.	0	0	0	0	0	Lg.	0	0	0	82	12	97	109	74
20/100	20/50	0	0	0	0	++	0	R.	0	0	0	79	12.2	94	104	44
.....	.....	0	0	0	0	0	0	0	0	0	0	81	11.8	76	98	50
20/20	20/20	0	0	0	D.	0	0	Lg.	0	0	0	89	12.4	89	111	31
20/20	20/30	0	0	0	D.Ir.	++	0	R.	0	0	W.S.	80	12	82	100	57
20/20	20/20	0	0	0	0	0	0	R.	0	0	0	93	15	96	107	69
20/30	20/70	0	0	R.	0	+	0	R.	0	0	0	81	12.2	86	101	79
20/20	20/20	0	0	R.	0	++	0	0	0	0	0	80	12.4	87	99	55
20/30	20/30	0	0	R.	D.	0	0	R.	0	0	0	40	8.2	95	89	58
20/20	20/30	0	0	0	D.	0	0	0	0	0	0	70	10.6	100	113	68
20/30	20/30	0	0	++	D.Ir.	+	L. +	R.	0	0	0	78	11.4	89	103	84
20/20	20/20	0	0	0	0	+	0	0	0	0	0	82	11.6	81	102	56
20/20	20/20	+C.	0	++	D.Ir.	+	0	0	0	0	0	87	12.4	89	109	72
20/20	20/20	0	0	0	0	+	0	0	0	Fur.	St.	97	12.6	82	113	94
20/20	20/20	0	0	+	D.	+	0	0	0	0	0	71	10.6	88	96	57
20/20	20/20	0	0	0	0	0	0	0	0	0	0	91	12	74	104	49
20/40	20/50	0	0	0	D.	+	+	Lg.	0	0	0	51	9	93	89	84
20/20	20/20	0	0	R.	0	0	0	0	0	0	0	89	12.6	91	113	63
.....	.....	0	0	0	0	+	0	0	0	0	W.S.	83	11.8	91	109	84
.....	.....	0	0	0	0	+	+	0	0	0	0	68	10.4	97	108	65
20/20	20/20	0	0	+	D.	++	0	Lg.	0	0	W.S.	80	11.2	100	121	85

	No.	Offense	Actual Age		Height		Height Percentile	Weight		Weight Percentile	Grip		Grip Percentile		Head		
			Yrs.	Mos.	In.	Mm.		Lbs.	Kg.		Right Kg.	Left Kg.	Right	Left	Girth, Cm.	Excess, Cm.	Deficit, Cm.
Dull Normals	1	Stealing	14	7	66	1,680	91	133¼	60.4	94	43	30½	92	73	56.5	2.2	....
	2	Stealing	14	5	56	1,425	09	87½	39.5	27	25	22	35	25	50.3	....	3.8
	8	Dependent	12	7	54⅞	1,395	36	71¾	32.5	27	23	19½	60	45	50	....	3.3
	16	Stealing	16	..	56	1,425	00	89¼	40.4	05	31	24	13	08	50	....	5.0
	17	Burglary	15	5	62⅛	1,580	37	114½	51.8	58	32½	36	41	63	53.3	....	1.4
	18	Incorrigible	10	7	54¾	1,392	83	80¾	36.6	91	25	24	93	96	52.5	....	0.3
	24	Truancy	11	4	57½	1,462	91	102¾	46.6	96	22	21	75	80	53.7	0.7	....
	25	Dependent	9	..	53¼	1,355	86	70¼	31.8	90	11	16	09	70	52.7	0.3	....
	33	Dependent	9	1	56⅛	1,430	95	81⅞	36.7	97	22	18	92	83	54	1.0	....
	36	Truancy	11	8	56⅛	1,427	81	75¾	34.3	70	23½	21	83	80	50.2	....	2.9
	46	Truancy	11	8	56½	1,437	84	70¾	32.5	54	19	20	50	70	52.5	....	0.6
	48	Dependent	10	..	54	1,372	76	74½	33.8	87	19	19	70	80	50.9	....	1.8
	54	Truancy	14	3	60¼	1,532	45	111½	50.5	78	40	35	90	87	56.9	2.9	....
	55	Dependent	14	3	60⅝	1,542	47	106	48.0	70	37	34	84	85	55	1.0	....
	56	Truancy	14	2	57	1,450	14	83¼	37.7	19	23	24	23	35	52	....	2.0
	71	Stealing	15	8	63⅜	1,615	50	129¾	58.8	84	44	43	82	87	56.3	1.5	....
	75	Dependent	16	8	63⅝	1,620	31	127¼	57.7	63	39	38	40	50	55.5	....	....
	77	Stealing	14	..	57⅛	1,452	15	88	39.9	29	30	28	60	60	52.7	....	1.2
	80	Truancy	15	1	62¾	1,595	42	115¾	52.4	61	35	30	50	40	54	....	0.5
	84	Truancy	13	4	54⅜	1,385	08	77¾	35.2	21	23	21	40	40	54	0.5	....
	90	Stealing	13	..	57⅝	1,465	41	88¾	40.2	57	24	23	45	50	53.3	....	....
	103	Stealing	13	8	62¼	1,585	86	128	58.0	94	28	31	70	90	53.5	....	....
	105	Dependent	13	6	61⅝	1,565	82	109¼	49.5	90	34	39	90	94	51.3	....	2.3
	109	Incorrigible	12	3	54½	1,385	32	87	39.4	76	21	17	40	20	52.3	....	0.9

—AND MENTAL FINDINGS—(*Continued*)

Vision		Strabismus	Defective Hearing	Enlarged Tonsils	Teeth	Lymph Nodes		Prepuce	Testes	Skin Disease	Postural Defects	Point Scale Score	Binet Age	Normal = 100		Physical Percentile (Normal = 50)
O. D.	O. S.					Cervical	Epitrochlear							Binet I. Q.	Point Sc. I. Q.	
20/20	20/20	0	+	R.	D.	+	0	R.	0	0	0	78	11	75	98	88
20/20	20/20	0	0	0	D.	+	+	0	0	0	0	64	11	76	80	24
20/20	20/20	0	0	0	D	+	0	Lg.	0	0	0	73	10	79	97	42
20/30	20/70	0	+	+	D.M.	0	0	R.	0	0	W.S.	84	12.2	76	99	07
20/30	20/200	+C.	0	R.	0	0	+	0	0	0	....	82	12.2	79	100	50
20/20	20/20	0	0	0	0	0	0	R.	Cry.	0	W.S.	53	9.2	87	85	91
20/30	20/40	0	0	0	0	+	0	0	Cry.	0	0	59	9.8	86	88	86
20/30	20/20	0	0	+	D.	+	0	Lg.	0	0	0	38	7.8	87	73	64
20/30	20/30	+C.	0	+	D.	++	L. +	Lg.	0	0	0	48	8.6	95	91	92
20/30	20/30	0	0	0	D.	+	0	0	0	0	0	59	10	85	83	79
.....	.....	0	+	R.	D.	++	L. +	R.	0	0	W.S. L.C.	63	10.6	91	88	65
20/20	20/30	+C.	0	0	D.	+	+	0	0	0	0	54	9.4	94	90	78
20/20	20/20	0	0	0	0	++	+	R.	0	0	0	74	10.4	73	92	75
20/20	20/30	0	0	++	D.	++	+	0	0	0	0	74	10.6	74	92	72
20/20	20/20	0	0	+	0	++	0	Lg.	0	0	0	70	11.2	79	88	23
20/200	20/20	0	0	0	D.	+	0	0	0	0	0	80	11.4	73	96	76
20/20	20/30	0	+	+	D	+	0	R.	0	0	0	80	12	72	91	46
20/30	20/30	0	0	+	0	+	++	0	0	0	W.S.	77	11	79	96	41
.....	.....	0	0	+	D.	++	0	0	0	0	0	79	10.6	70	98	48
20/20	20/20	0	0	+	D.	+	0	Lg.	0	0	0	71	11	83	92	27
20/20	20/20	0	0	0	0	0	0	R.	0	0	0	74	11	85	97	48
20/20	20/30	0	+	R.	Ir.	++	0	0	0	0	0	72	11.4	83	91	85
20/20	20/20	0	0	0	0	+	0	0	0	0	0	71	10.8	80	91	89
20/20	20/30	0	+	+	0	++	0	R.	0	0	0	66	10.6	86	89	42

TABLE 2.—Summary of Physical—

	No.	Offense	Actual Age		Height		Height Percentile	Weight		Weight Percentile	Grip		Grip Percentile		Head		
			Yrs.	Mos.	In.	Mm.		Lbs.	Kg.		Right Kg.	Left Kg.	Right	Left	Girth, Cm.	Excess, Cm.	Deficit, Cm.
Borderlines	11	Stealing	15	10	63⅞	1,625	57	119¼	54.1	69	31	30	35	40	55	....	....
	12	Stealing	14	2	58¼	1,477	24	96¾	43.8	49	31	35	65	88	55	1.0	....
	13	Dependent	12	..	55¾	1,420	49	76¾	34.8	48	20	18	30	30	50	....	3.2
	23	Truancy	15	..	60⅛	1,530	18	105¾	47.9	35	26	22	10	09	52	....	2.5
	31	Burglary	15	9	60½	1,540	21	119	53.9	68	32	29	40	35	.....	....	....
	34	Dependent	15	9	60¼	1,535	19	122¾	55.6	78	37	32	57	50	53	....	1.9
	49	Stealing	16	4	65	1,652	41	133	60.3	75	....	....	....	....	55.7	0.5	....
	50	Dependent	14	7	59½	1,512	47	110	49.8	76	32	26	70	50	54.5	0.8	....
	58	Stealing	12	5	49⅛	1,250	0	60¼	27.2	06	15	15	07	10	54	0.7	....
	70	Burglary	15	8	60⅞	1,550	25	117½	53.2	65	37	32	57	50	54	....	0.8
	74	Burglary	14	3	59¾	1,492	30	92½	41.8	39	30	28	60	60	56	....	2.0
	85	Incorrigible	14	2	53½	1,360	05	72¼	32.7	07	23	23	23	30	50	....	1.1
	86	Incorrigible	10	..	49¼	1,252	09	64¼	29.1	46	21	19	85	80	51	....	1.7
	94	Stealing	16	4	63¼	1,610	26	117	53.0	39	41	35	50	35	53	....	2.2
	95	Incorrigible	14	8	66¼	1,685	92	135½	61.4	95	37	28	84	60	53	....	1.4
Morons	7	Stealing	18	9	61⅞	1,575	—7	106¾	48.4	05	36	28	00	—8	56	0.3	....
	32	Stealing	17	..	65½	1,665	32	124	56.2	36	42	41	36	43	53	....	2.6
	45	Incorrigible	17	6	63¾	1,620	14	125½	56.8	38	24	29	03	08	51.5	....	4.1
	51	Incorrigible	12	10	53⅛	1,350	16	74¾	33.8	42	22	20	50	50	52	....	1.3
	52	Incorrigible	14	3	55	1,400	07	82½	37.4	18	21	19	10	10	50.5	....	3.5
	60	Truancy	17	2	62½	1,590	09	111	50.3	13	35	34	10	17	54	....	1.5
	73	Incorrigible	17	3	60⅞	1,550	08	108½	49.2	10	36	31	11	09	53	....	2.5
	93	Truancy	16	..	61⅜	1,560	12	126	57.2	59	38	36	37	40	57	....	2.0
	96	Truancy	13	9	52⅜	1,382	08	71¼	32.3	08	42	23	93	50	50.1	....	3.6
Imbeciles	3	Truancy	19	4	56⅞	1,445	—2	93½	42.3	—9	24	23	—26	—15	.....	....	....
	21	Incorrigible	16	3	65	1,652	41	143	64.8	87	41	44	50	77	55.2	....	....
	53	Incorrigible	8	5	46⅛	1,172	15	51¾	23.4	33	10	16	10	86	50	....	2.2
	101	Incorrigible	10	7	52⅝	1,337	55	87	39.4	93	11	7	07	—2	54.5	1.7	....

W.S. = Wing scapulae
E. = Defective enamel
Im. = Impetigo

Lg. = Elongated prepuce
Fur. = Furunculosis
L. = Left

D. = Decay
St. = Stoop shoulders
L.C. = Lateral curvature of spine

Vision		Strabismus	Defective Hearing	Enlarged Tonsils	Teeth	Lymph Nodes		Prepuce	Testes	Skin Disease	Postural Defects	Point Scale Score	Binet Age	Normal = 100		Physical Percentile (Normal = 50)
O. D.	O. S.					Cervical	Epitrochlear							Binet I. Q.	Point Sc. I. Q.	
20/20	20/30	0	0	0	0	++	0	Lg.	0	0	0	64	11	70	75	50
20/20	20/20	0	0	0	D.	0	0	0	0	0	0	55	9.6	68	69	57
20/30	20/30	C. +	0	+	D.	+	0	Ph.	Cry.	0	0	46	9	75	62	39
20/20	20/20	0	+	++	D.	+	0	0	Cry.	0	W.S.	65	10.6	71	81	18
20/20	20/20	0	0	R.	D.	+	+	R.	0	0	L.C.	60	10.6	67	72	41
20/30	20/40	0	+	++	D.	+	0	R.	0	0	L.D.	64	10.4	66	77	51
20/200	20/50	0	0	0	D.	0	0	0	0	0	0	78	11.8	72	91	
20/20	20/20	0	0	+	0	+	0	0	0	0	St.	59	9.8	67	73	61
20/50	20/40	0	0	R.	0	+	+	Lg.	0	0	0	51	9.4	76	68	06
20/20	20/20	0	0	+	D.	+	0	0	0	0	0	64	10.8	69	76	49
20/20	20/30	0	0	+	D.	+	+	Ph.	0	0	0	62	10.4	73	78	47
20/20	20/20	0	0	R.	D.	0	0	0	0	0	0	69	10.2	72	86	16
20/30	20/30	0	0	0	D.	++	0	0	0	0	0	51	8.6	86	85	55
20/20	20/20	0	0	0	0	++	0	0	0	0	0	70	11	68	81	36
20/20	20/40	0	0	++	0	++	0	Lg.	0	0	0	64	10.4	71	80	83
20/30	20/100	0	0	0	D.	0	+	0	0	0	St.	55	9.4	50	58	—3
20/30	20/30	0	+	0	D.	0	0	0	0	Im.	St.	35	7.4	44	39	37
20/40	20/40	0	0	0	D.	0	0	0	0	Fur.	0	47	8.8	50	50	16
20/20	20/20	0	0	+	0	+	0	R.	0	0	0	36	8.4	66	47	40
20/40	20/30	0	0	0	0	+	0	R.	0	0	0	35	8	56	44	11
20/40	20/40	0	0	0	0	0	0	R.	0	0	W.S.	38	7.2	42	42	12
20/100	20/100	+C.	+	0	0	0	0	0	0	0	0	59	10	58	65	10
20/30	20/70	0	++	+	0	0	0	0	0	Acne	0	63	10.2	64	74	37
20/30	20/30	0	+	0	0	+	0	0	0	0	0	39	8	58	49	40
20/20	20/30	0	+	0	0	0	0	0	0	0	St.L.C.	15	6.4	33	16	13
20/40	20/50	+D.	0	0	D.	0	0	0	0	0	0	22	6.6	40	26	64
.....	.....	0	0	+	D.	+	0	Lg.	0	0	W.C.	17	5.4	64	39	36
.....	.....	0	0	0	D.	++	0	0	0	0	0	15	4.4	24	24	35

C. = Convergent
Cry. = Cryptorchidism
Ld. = Lordosis

D. = Divergent
M. = Malocclusion
R. = Removed

Ir. = Irregular
Ph. = Phimosis

TABLE 3.—SUMMARY OF PHYSICAL EXAMINATIONS

	Cases						
	Normal	Dull Normal	Borderline	Moron	Imbecile	Total Normal	Total Defective*
Number of cases	41	24	15	9	4	65	28
Average height percentile	52.7	52.6	30.8	11.0	27.8	52.7	23.1
Average weight percentile	52.7	63.7	53.0	25.4	51.0	56.7	43.9
Average right grip percentile	66.3	59.4	48.1	27.8	10.3	62.7	34.4
Average left grip percentile	70.5	63.0	44.8	24.8	36.5	66.6	35.4
General percentile average	60.6	59.7	44.2	22.1	31.8	59.7	34.2
Minimum height percentile	8	0	0	—7	—2		
Maximum height percentile	96	95	92	32	55		
Variation	88	95	92	39	57		
Minimum weight percentile	8	5	6	5	—9		
Maximum weight percentile	94	97	95	59	93		
Variation	86	92	89	54	102		
Minimum right grip percentile	2	9	7	0	—26		
Maximum right grip percentile	102	93	85	93	50		
Variation	100	84	78	93	76		
Minimum left grip percentile	9	8	9	—8	—15		
Maximum left grip percentile	110	96	88	50	86		
Variation	101	88	79	58	101		
Head girth deficit	0.5	0.7	1.0	2.7	0.2	0.6	1.4
Percentage cases with							
Vision below 20/30, O. D.	11.8	4.5	13.3	45.4	50.0	8.9	26.9
Vision below 20/30, O. S.	11.8	13.6	26.7	45.4	50.0	12.5	34.6
Strabismus	7.3	12.5	6.7	11.1	25.0	9.2	10.7
Defective hearing	2.4	25.0	13.3	45.4	25.0	10.8	25.0
Hypertrophied tonsils	24.4	41.7	46.6	22.2	25.0	30.8	35.7
Tonsils removed	9.8	12.5	20.0	0	0	10.8	10.7
Tonsils removed or hypertrophied	34.2	54.2	66.7	22.2	25.0	41.6	46.4
Dental defects	48.8	62.5	66.7	33.3	75.0	53.8	57.2
Enlarged cervical glands	58.6	83.3	75.0	33.3	50.0	67.3	60.8
Enlarged epitrochlear glands	14.7	33.3	20.0	11.1	0	21.6	25.0
Skin disease	17.1	0	0	33.3	0	10.8	10.7
Postural defects	19.5	16.7	26.7	33.3	50.0	18.5	31.2

* Including borderlines.

The physical percentile (general average) was obtained by averaging the percentiles for height, weight and right and left grip and therefore is comparable with the "psychophysical" percentile of Doll,[7] except that he included also the figure for vital capacity. The reader is again reminded that the norm for the intelligence quotient is 1.00, and for all percentiles is 50. The averages in the small imbecile group are unduly influenced by a single physically exceptional case.

The chief feature of our results, that the physical group average is proportional to the mental status of the group, is in agreement with the work of Porter, Christopher, Smedley, Doll and many others (see Doll's monograph[7]), but we should like to emphasize again, by reference to our figures, that this is true of groups only. For instance, nineteen of our forty-one normal cases (46.4 per cent.) showed height percentiles below 50. On the other hand, one imbecile and three borderlines (14.6 per cent.) out of the defective groups were above 50 for height. Seventeen of the dull normal and normal groups (26.2 per cent.) were below 50 for weight, while ten (35.7 per cent.) of the defectives were above 50. Eighteen (27.8 per cent.) of the normal groups were below 50 for right grip, and fourteen (21.6 per cent.) for left grip, while of the defective eleven (39.3 per cent.) were above 50 for right grip and twelve (42.8 per cent.) for left grip. These facts do not affect the fact of physical inferiority in mental defectives as a *group*, but it certainly rules out any diagnostic value in physical measurements for mental capacity.

Certain special phases of the physical examination could be related to mental status. In the dull normal group it will be seen that the percentage of boys with hypertrophied tonsils and chronic lymphadenitis (probably also with adenoid growths) was much larger than in the normal group, and this fact may be of considerable significance in explaining retardation.

Faulty vision[8] was found more frequently in the retarded and defective groups than in normal groups. This confirms Burpitt's[9] observations. Only 8.9 per cent. of our normals had less than 20/30 vision for the right eye, and 12.5 per cent. for the left, while 26.9 per cent. of the defectives had less than 20/30 for the right, and 34.6 per cent. for the left. The differences between the normal and dull normal groups for vision are not striking. Defective hearing, on the other

7. Doll, E. A.: Anthropometry as an Aid to Mental Diagnosis. Publications of the Training School at Vineland, N. J. Research Dept. No. 8, February, 1916.

8. For summaries of previous work on the special senses in defectives the work of Whipple (Manual of Mental and Physical Tests, Baltimore, Warwick and York, 1914, Part 1) should be consulted.

9. Burpitt, H. R.: Mental Retardation, Nutrition and Eyesight in School-children. Ophthalmoscope, 1915, **13**, 442.

hand, was found in 25 per cent. of the dull normals as against 2.4 per cent. for the normals, a highly suggestive fact. For the normal group as a whole 10.8 per cent. showed defective hearing, as compared with 25 per cent. for the defectives.

Postural defects were also more frequent in the defectives, occurring in 31.2 per cent. and in only 18.5 per cent. of these normals. This observation has, we believe, not been made before.

Other physical abnormalities, such as dental caries, cervical and epitrochlear adenitis, genital defects and skin disease, are about evenly distributed between the normal and defective groups.

OFFENSES

In a group of eighty-five boys not committed for dependency or neglect, the offenses were distributed as shown in Table 4.

TABLE 4.—Distribution of Offenses

	Stealing	Truancy	Incorrigibility	Burglary
Normals	20	5	7	4
Dull normals	7	9	5	0
Borderlines	6	2	2	4
Morons and imbeciles	3	4	7	0

Stealing and burglary formed 54.5 per cent. of the offenses in the normal groups and 46.4 per cent. in the defective groups, not a striking difference.

HOME CONDITIONS

In the case of defectives, feeblemindedness is in itself a sufficient explanation of delinquency. In the case of normal children, however, it was believed that a study of environment might have considerable sociologic interest. Such an investigation was carried out by Miss Rosenshine in the case of fifty-five of our normal or dull normal groups, and is summarized in Chart 5. We do not care to make a detailed analysis of these findings, leaving this task to more experienced interpreters of social conditions, but we may point out that in nearly every case the home conditions were very unfavorable; this and the lack of home influence of any kind are important contributing causes of juvenile delinquency.

A frequent problem with which we have met is the case of the children of immigrants, especially of the non-English speaking class. It frequently happens that the parents have failed to adapt themselves to their new environment and their children suffer the double handicap of poverty and the conflict, expressed in many ways, between old and

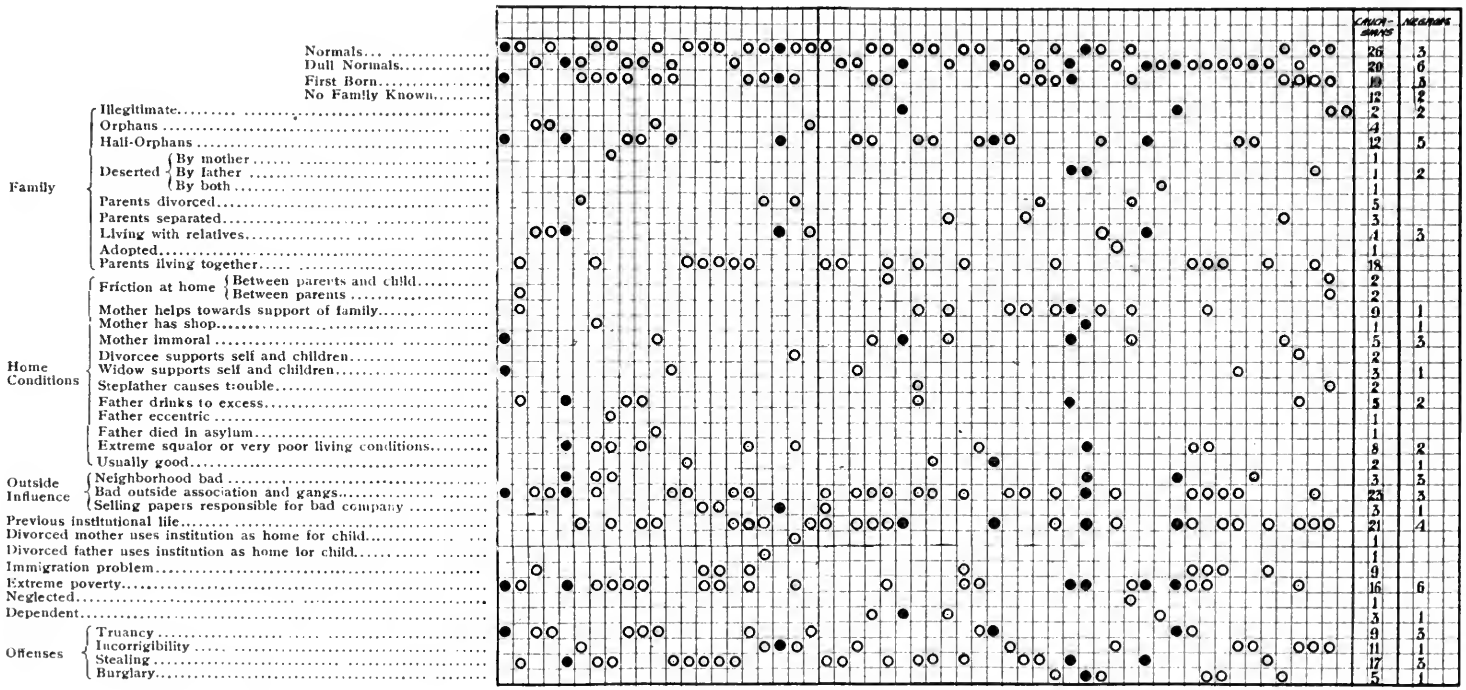

Chart 5.—Summary of environmental conditions, normal and dull-normal groups. Whites = ○; negroes = •.

new world modes of life. This means in nearly every case the loss of home influence.

The frequency of illegitimacy, prostitution, divorce, and heavy drinking in the families investigated also deserves mention.

CONCLUSIONS

Our survey is of a group of juvenile offenders, and so is of importance as reemphasizing the physical, mental and moral problems which the community must solve before it can hope to deal helpfully with the problem of delinquency. The physical findings are, on the whole, those of neglected hygiene, secondary in most cases to poverty. The mental findings show that of the boys studied 43.6 per cent. were normal, 25.5 per cent. dull normal (total normals 69.1 per cent.), 17 per cent. borderline, 9.6 per cent. morons, and 4.3 per cent. imbeciles (total defectives 30.9 per cent.). A study of the normal and dull normal groups brings to light various unfavorable home conditions. We cannot avoid the conclusion that for the normal boys improved environment, improved personal hygiene, and better general education would have made useful citizenship possible.

In any group such as the one with which we have dealt, the first indication is obviously to separate the normals and dull normals from the rest, to keep the borderline cases under observation, with careful and systematic attempts at education in order to determine and develop latent ability; and finally to segregate promptly those who are beyond question feebleminded.

Of these problems the reeducation of normal individuals who have become delinquent is at once the most difficult, the most hopeful and the most important. Without special and extremely capable training these boys, who have potentialities not only of "floating" in society and of becoming good citizens, but even, in some instances, of attaining positions of superiority, will inevitably return to a career of delinquency or crime from which at a slightly later age it will be impossible to rescue them. Any institution such as the one we have studied must choose whether it will be a place of intelligent rehabilitation or a feeder to the criminal class.

About half the physical examinations were made by Dr. H. H. Yerington and Dr. W. L. Adams, and several special eye examinations were performed by Dr. Hans Barkan. For these, grateful acknowledgement is made.

THE CAUSE OF SUDDEN DEATH IN STATUS LYMPHATICUS *

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Status lymphaticus is a constitutional hereditary anomaly characterized anatomically by certain external peculiarities of configuration, by hypoplasia of the cardiovascular apparatus, by hyperplasia of the thymus gland and of the lymphoid tissues in other localities, and, incidentally, by congenital structural defects in different viscera. Clinically, the condition is not infrequently terminated by sudden death on apparently trivial provocation, oftenest in children, but occasionally in adults.

Among the first to recognize the anatomic defects in status lymphaticus and to apply their visible manifestations to purposes of diagnosis during life were Dr. Charles Norris in New York and Neusser in Vienna. Clinically, the condition may be identified in the living male subject by bodily configuration simulating that of the female. The face is beardless, or nearly so, and the axillary and other hairs are scanty, the skin is smooth and unusually delicate, the pubic hairs are sharply defined in a transverse direction, the waist is narrow, and the thighs are gracefully arched. In the female the diagnosis during life is rather more difficult, and rests largely on features which are but an accentuation of those normally encountered, namely, the thin, delicate skin, the narrow waist and the arched thighs, together with the small axillary fat pads and the scanty growth of hair on them.

The anatomic changes in the deeper parts are of practical significance. Among the first 4,000 necropsies at Bellevue Hospital status lymphaticus was encountered in 249 subjects, or in 6.2 per cent.; 197 times in males and 52 times in females. In our necropsy protocols we are accustomed to describe two types — status lymphaticus and status lymphaticus recessivus. In the Bellevue Hospital cases, 118 examples of status lymphaticus were encountered, and 89 cases belonging to the recessive type. In 42 instances border line cases were observed.

The anatomic changes were distributed thus:

Status Lymphaticus. — Of 118 cases of straightforward status lymphaticus the thymus was enlarged in every case. The weight of

* Submitted for publication Oct. 7, 1917.

* From the Pathological Laboratories of Bellevue and Allied Hospitals; Director, Dr. Charles Norris.

the thymus was recorded 66 times. The youngest subject was a child of 8 hours whose thymus weighed 70 gm. The oldest subject was 38 years of age and the thymus likewise weighed 70 gm.

The average weight of the thymus, grouped according to years, was as shown in the table.

Table of Average Weights in Status Lymphaticus

Age, Years	Average Weight, Gm.	No. of Cases
Under 1	25.0	13
1- 5	18.0	14
6-10	24.0	5
11-25	22.0	5
16-20	23.0	9
21-30	27.8	17
31-40	33.8	3

Of the 118 cases, the faucial tonsils were enlarged 61 times (51.7 per cent) ; the lingual tonsils 58 times (49. per cent) ; the pharyngeal lymphoid follicles 45 times (38 per cent.). Peyer's patches and the solitary follicles were each enlarged 105 times (89 per cent.). The axillary nodes were enlarged 11 times (9 per cent.) ; the inguinal nodes 12 times (10 per cent.), and the cervical nodes 15 times (12.8 per cent.).

The spleen was small or normal in size in 68 cases (70 per cent.) ; the Malpighian follicles were hyperplastic 101 times, or in 85 per cent.

Status Lymphaticus Recessivus.—This is attended by retrogression of the lymphoid tissues, the other anatomic anomalies remaining, of course, unchanged. The recessive condition is encountered oftenest in individuals who have passed the twentieth year. Rarely is it seen before that age. It is attended by recessive changes in the lymphoid follicles varying in both location and extent, the most frequent indication of regression being found in the follicles of the intestinal tract, where atrophic changes occur in inverse proportion to the hyperplastic alterations in status lymphaticus, and in the thymus gland, which, in well marked instances, is practically completely replaced by fat. In the case of the lymphoid follicles of the intestine, lymph nodes and spleen the recessive changes are ascribable partly to natural involution and partly to connective tissue replacement of the germinal follicles, the latter process striking at the source where lymphoid cells are regenerated, while in the case of the thymus, recession is almost entirely an involutional change.

Of 89 cases of recessive status lymphaticus the thymus was weighable 19 times, and the average weight was 18 gm. In the remaining 70 cases (78.6 per cent.) the thymus was completely replaced by fat.

Of the 89 cases of recessive status lymphaticus the faucial tonsils were hyperplastic 25 times (28 per cent.) ; the lingual tonsils 32 times (36 per cent.), and the pharyngeal tonsils 19 times (21 per cent.).

Peyer's patches were atrophied 61 times (68.5 per cent.) and the solitary follicles 37 times (41 per cent.). The splenic follicles were enlarged 37 times (41 per cent.) and atrophied 39 times (43.9 per cent.). The spleen was normal or small in size in 52 cases (71 per cent.).

Of the 249 cases of status lymphaticus the heart was small 127 times (51 per cent.), and in 101 cases (40.5 per cent.) the aorta was diminished in caliber, 71 times by actual measurement. In 78 cases (31 per cent.) the elasticity of the aorta was increased, and in 66 cases (26.5 per cent.) the vessel was described as unusually thin.

The practical application of the anatomic changes in status lymphaticus may be described under two heads:

Anatomic Changes.—The external configuration of the body is of great importance, since it serves at once to identify individuals, especially children, who are to be watched with the utmost care in order that they may be safely guided through events which, ordinarily, are free or relatively free from danger. To them the trivialities of life are apt to assume the magnitude of perils — vaccination, the injection of antitoxin, thoracentesis, light anesthesia, submersion—any one of these or their like may eventuate in sudden death. Moreover, children of this type are not only unusually susceptible of infection, but they bear infection badly, a clinical fact which was long ago recognized by the elder Gross when he described the "angelic child"—fair haired or dark, blue eyed or brown, thin lipped, pink cheeked, alert to the point of precocity, with velvety skin, thin, long bones, shapely limbs and graceful movements — born beautiful, but a prey to infection and a bad risk.

In adult life status lymphaticus is of interest from a sociologic as well as from a medical standpoint. Thus it is of striking frequency among individuals of unstable emotional qualities, including alcohol and other drug habitués (Emerson), criminals and suicides (Norris, Schultze, Symmers, Bartels), neurasthenics and savages (Symmers), epileptics and the insane (Karpas), and subjects of such glandular perversions as Addison's disease, exophthalmic goiter, acromegalic giantism and other forms of pituitary disease.

Sudden Death.—Sudden death in subjects of status lymphaticus has often been ascribed to pressure of the enlarged thymus on the trachea, but those who have most carefully studied the condition postmortem do not hold to this view; in fact, the theory is now credited in few quarters. At Bellevue Hospital we have never been able to implicate the enlarged thymus as a mechanical factor in the production of death. On the contrary, sudden death in status lymphaticus is an exceedingly subtle procedure, and is most logically explicable, I believe, by the laws

of anaphylaxis as promulgated by the experimental pathologists and exemplified by certain types of disease in man. This opinion is based on anatomic and histologic observations. Thus, the lymphoid tissues are most abundantly developed in youth and early adolescence, and undergo diminution as age advances — an observation which assumes importance in view of the fact that in status lymphaticus the danger of sudden death is greatest during that period of life in which the lymphoid tissues are most flourishing, and is practically unknown in the recessive stage. It is likewise significant that, in status lymphaticus, those lymphoid tissues which display the highest degree of hyperplasia are to be found in the mucous membrane of the gastrointestinal tract where, of all the lymphoid structures, they are the ones most actively engaged in the process of filtration, in the course of which they are constantly subjected to the destructive action of a great variety of toxic substances, both chemical and bacterial. It is important to note, therefore, that, in children suddenly dead with all the physical attributes of status lymphaticus, microscopic examination of the lymphoid tissues throughout the body reveals constant and characteristic changes in the germinal follicles in the form of necrotic lesions marked by excessive disintegration of nuclei and the formation of "nuclear dust." These changes may be demonstrated in myriads of follicles; in fact, it is rarely possible in these circumstances to find a follicle that is intact. In other words, the histologic changes in question tend to show that sudden death in status lymphaticus is in some way connected with the release of nucleoproteins formed as a result of destruction of innumerable germinal follicles. It is scarcely conceivable, however, that death is directly traceable to the sudden and simultaneous destruction of a large number of follicles, since the interval between injury and death is far too short, in the majority of cases, to permit so many necrotic lesions to occur throughout such a wide distribution. It is more probable, I think, that death is of the nature of an anaphylactic phenomenon, sensitization being expressed in structural terms by the necrotic germinal follicles and, chemically, by the release of nucleo-proteins which, although not strictly foreign, are none the less pathologic, and comparable, in a toxicologic sense, to alien products. Previous to the expiration of the so-called anaphylactic incubation period the lymph nodes are subjected to the action of destructive substances which serve to bring about still further disintegration of germinal nuclei, thus providing the requisite quantity of specific protein to complete the anaphylactic reaction. The destructive substances in question may be introduced in the form of antitoxins hypodermically injected, or as vaccines applied by scarification or otherwise, or as substances derived from intestinal absorption, or manufactured in the

process of shock induced even by such simple procedures as the prick of a needle, sudden exposure to cold, and a number of similar events. That apparently trivial and negligible affairs are sometimes attended by extraordinary physical or chemical revulsions is a recognized fact in medicine, and is illustrated, among other things, by the almost instantaneous jaundice which sometimes is occasioned by severe fright, so that the occurrence of equally remarkable reactions in status lymphaticus is by no means unprecedented.

That acute necroses may occur in irregular showers is shown by the presence of all stages of both the necrotic and reparative processes in the same lymph node and in different nodes of the same body. This fact is of moment, in that the anaphylactic reactivity of the body is determined by the number of acute necrotic lesions in the germinal follicles, or, in other words, the anaphylactic incubation period in man, as in experimental animals, varies with the initial dose of the sensitizing protein. For example, in guinea-pigs injected with small amounts of horse serum, from twelve to fourteen days suffice for sensitization. With larger doses, however, the interval may be extended to weeks or even months. In subjects of status lymphaticus it is naturally to be expected that early sensitization follows a small shower of necroses and that larger showers are succeeded by a longer period of incubation, the reactive ranges thus varying within wide limits. At one moment the tissues are exquisitely tuned and await only the receipt of a sufficient quantity of specific protein to react fatally, while at another moment events are so timed that the same quantity of specific protein exerts no such effect, a fact which tends to explain why certain subjects of status lymphaticus survive procedures which, in others, are attended by disaster. In this instance it is apparently a question of anaphylactic reactivity dependent on the number of acute necrotic lesions in the lymph nodes and on the interval that has elapsed since their inception. In other circumstances, however, immunity from sudden death in status lymphaticus seems to be due to the process of so-called anti-anaphylaxis, which may be produced artificially in animals by injecting them, before the expiration of the anaphylactic incubation period, with a single large dose of the same foreign protein which was used for purposes of sensitization. The animal recovering from the symptoms induced by the second injection is thereafter immune to the effects of the same protein. Precisely the same process seems to occur in status lymphaticus when, following sensitization to a specific protein and before the anaphylactic incubation period is over, the same protein is formed in larger quantities following a shower of necroses in the germinal follicles. After this the individual is immune and is enabled to withstand not only trivial

shocks, but even perils of great magnitude, such as infections, major accidents and operations demanding deep anesthesia. This interpretation is borne out by the fact that, in subjects of status lymphaticus, especially adults, in whom death is attributable to causes other than anaphylaxis, acute necrotic changes in the germinal follicles of the lymph nodes are exceedingly rare, or may not be demonstrable at all, the vast majority of the follicles exhibiting, on the contrary, definite signs of connective tissue replacement, showing that necrotic lesions have been present at some time, but have been repaired.

It is quite possible, on the other hand, that in certain cases of status lymphaticus the phenomenon of allergy obtains; that is to say, the patient is hypersensitive to the effects of a second dose of the specific protein with which he has been sensitized, in which event one shower of follicular necroses following rapidly on another might readily give rise to a fatal reaction, or, failing this, to certain of the lesser phenomena to which subjects of status lymphaticus are liable, and which vary in intensity from simple urticarial rashes to convulsive disorders. It is along this line of procedure, I think, that we must seek to obtain a comparatively harmless diagnostic test which will indicate to what extent, if any, a given patient is susceptible to the effects of nucleoproteins derived from the destruction of lymphoid cells.

Finally, it is significant that, in guinea-pigs, death from anaphylaxis is accompanied by asphyxia due to tetanic spasm of the muscles in the smaller bronchi, and similar changes in human beings are undoubtedly responsible for such respiratory phenomena as asthmatic attacks, etc. Sudden death in status lymphaticus is likewise a respiratory event, directly traceable, however, not to peripheral causes, but most likely, to disturbances of the respiratory center in an individual whose nervous, vascular and lymphatic systems are notoriously unstable.

A second and less subtle cause of sudden death in status lymphaticus sometimes occurs in young adults as a direct result of rupture of a peripheral or central cerebral artery spontaneously, or on apparently trivial traumatism. A number of cases of this description have been observed in the past ten years in the necropsy room at Bellevue Hospital. Many of them were of profound medicolegal importance. In this type of case the subject always presents the bodily configuration and the other anatomic features of status lymphaticus, and necropsy reveals unusually delicate cerebral vessels, the deficiency being most noticeable in the muscular coat, rupture occurring apparently under the influence of excitement, exertion or other cause of sudden elevation of blood pressure. For example, in a case recently investigated postmortem by Dr. O. H. Schultze, the subject died suddenly while engaged in a fisticuff, and death was found to be due to spontaneous rupture

of an hypoplastic meningeal vessel, the party of the opposite being thus saved from a probable conviction on the charge of manslaughter.

CONCLUSIONS

Sudden death in status lymphaticus may be brought about in at least two different ways. The first and most frequent cause is of the nature of an anaphylactic reaction due to sensitization of the body by a specific nucleoprotein formed in the lymph nodes as the result of necrosis of numbers of germinal follicles. Before the so-called anaphylactic incubation period has expired the tissues are again subjected to the action of the same protein formed in the same type of tissue in response to an apparently trivial injury, and, in this way, the anaphylactic reaction is completed.

A second cause of sudden death in status lymphaticus is to be found in the form of spontaneous rupture of an hypoplastic cerebral vessel, or rupture following apparently trivial injury, the deficiency in the vessel wall being most noticeable in the muscular coat.

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THE TREATMENT OF SECONDARY ANEMIA IN INFANTS BY BLOOD TRANSFUSION *

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The cases covered in this report were referred to me because of simple secondary anemia or because of anemia and malnutrition. Various food combinations had been tried and all patients had received medical treatment for the anemia.

TECHNIC OF BLOOD TRANSFUSIONS

The transfusions were made at the Babies' Hospital by Dr. E. A. Morgan and Dr. T. C. Clark, former resident physicians of the hospital.

The blood of the donor was proved fit by the absence of agglutination and hemolysis.

The following instruments were used: Five record syringes, Lindemann needle, exploratory needle, hypodermic syringe with needle, scalpel, clamps, catgut, silk and needles.

The following technic was employed: The skin over the median basilic vein was cleaned and cocainized. An incision was made and about 2 cm. of the vein exposed and dissected free from the surrounding tissues. A small opening was made into one side of the vein with a pair of scissors, and a Lindemann needle inserted. The vein below the needle was then tied off and another suture was placed over the vein to hold the needle in place. A small amount of salt solution was introduced, to make sure that there was no leakage.

A rubber tourniquet was placed on the arm of the donor and the skin cleansed over the most prominent vein. The exploratory needle was inserted directly into the vein and the blood drawn with a record syringe until it was full. This syringe was then handed to the operator working on the child and the blood inserted into the child's vein. At the same time a fresh syringeful of blood was being obtained from the donor. Each syringe was well washed out with sterile salt solution before being used again to collect blood. This procedure was continued until the required amount had been transfused.

The immediate and later results are shown in the accompanying table.

The results in all but one patient were satisfactory. The patient in Case 4 was transfused twice, and in each instance there was improvement as shown by the blood examination, but it failed to hold longer than a few weeks. This child made a gain in weight, but the general improvement was not satisfactory. The abdomen was greatly distended, not unlike Hirschsprung's disease. In the other cases there was no return of the anemia and subsequent growth and development was all that could be hoped for.

Cases 5 and 7 require special mention. In addition to the anemia there was extreme malnutrition. The patient (Case 5) was very weak and exhausted to the point of development of small petechial hemor-

* Submitted for publication Sept. 10, 1917.

The Blood in Secondary Anemia Before and After Transfusion

Sex	Age, Months	Weight, Pounds	Blood Before Transfusion		Amount Trans-fused, C.c.	Blood After Transfusion						Weight, Pounds
			Hemo-globin, per Cent.	Red Blood Corpuscles		Hours After	Hemo-globin, per Cent.	Red Blood Corpuscles	Months After	Hemo-globin, per Cent.	Red Blood Corpuscles	
F.	12	12.5	14 (Sahli)	2,400,000	175	24	45 (Sahli)	5,120,000	17	70 (Fleischl)	4,600,000	26.8
F	18	24.0	37 (Sahli)	3,900,000	200	24	55 (Sahli)	5,760,000	14	90 (Fleischl)	5,000,000	32.0
M	12	16.4	32 (Sahli)	4,480,000	300	24	78 (Sahli)	5,150,000	8	60	3,840,000	19.5
									6	52	4,400,000	22.2
									12	63	5,000,000	25.5
									18	65 (Dare)	5,000,000	28.0
F.	23	15.10	20	2,800,000	140	24	55	3,100,000	1	37	2,700,000	16.7
	24	16.7	30 (Sahli)	....	200	24	90 (Sahli)	4.320,000	7	.. (Dare)	....	19.8
F.	6	11.0	37 (Sahli)	1,600,000	150	24	85 (Sahli)	4,000,000	7	65 (Dare)	4,800,000	19.5
M.	10	12.5	33 (Dare)	4,300,000	200	24	58 (Dare)	4,900,000	1	58 (Dare)	5,000,000	12.8*
F	12	12.4	35 (Sahli)	3,120,000	170	24	62 (Sahli)	4,040,000	1	50	5,320,000	14.0
									3	50	4,140,000	17.4
									6	56 (Dare)	4,400,000	19.8
M	16	21.0	35 (Sahli)	3,310,000	200	24	55 (Sahli)	3,400,000	1	60 (Dare)	4,500,000	24.8
									6	55 (Fleischl)	4,100,000	25.12

* Died of acute meningitis three months later.

rhages over the body, particularly over the lower abdomen. Several weeks of treatment were required to bring her to a reasonably normal condition. In Case 7 the patient was a very anemic twin and failed to grow regardless of the food given. She made a prompt and rapid response to transfusion.

The table shows the weight increase and the blood findings before and after transfusion, but it cannot record the marked change in the patients—the change from sickly, whiny infants into happy, apparently well infants. The patients were transformed from those with a digestive capacity barely able to maintain existence into those that took on the normal constructive processes of early life.

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